***** QUERY RESULTS *****

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=> d his l43

     (FILE 'HCAPLUS' ENTERED AT 09:21:58 ON 06 JUN 2007)
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=> d que l43
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                0/BI OR 773904-85-1/BI OR 773904-86-2/BI OR 773904-87-3/BI OR
                773904-88-4/BI OR 773904-89-5/BI OR 9036-21-9/BI)
L6         6777 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L7        25179 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ARTERY, DISEASE"/CT
L8        35151 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ATHEROSCLEROSIS/CT
L9        48956 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ATHEROSCLEROSIS/OBI OR
                ARTERIOSCLEROSIS/OBI
L10        9314 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ARTERIOSCLEROSIS/CT
L11       67514 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L7 OR L8 OR L9 OR L10)
L14        6717 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RESTENOSIS/OBI OR CORONARY
                RESTENOSIS/OBI
L15       68114 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 OR L14
L16         197 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 AND L15
L17     1429462 SEA FILE=HCAPLUS ABB=ON  PLU=ON  1/SX,SC
L18         162 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L17
L22       35469 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG SCREENING/CT
L23       38363 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG/OBI (2A) SCREEN?/OBI
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L25          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 AND L24
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                <2004 OR REVIEW/DT
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L34         113 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND L33
L35           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L24 OR L26) AND L34
L36          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 OR L25
L37           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L28
L38         113 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND L28
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L40          63 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 AND L39
L41        1066 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHODIESTERASE#/OBI (2A)
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L43          26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 OR L37 OR L42


=> d his l63

     (FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 09:39:41 ON 06 JUN 2007)
L63          32 S L62 AND L28

=> d que l63
L5            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  (773904-83-9/BI OR 773904-84-
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                773904-88-4/BI OR 773904-89-5/BI OR 9036-21-9/BI)
L6         6777 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-714137P P 20050902

ED Entered STN: 09 Mar 2007

AB The present invention relates to methods of using a G protein-coupled receptor (GPCR) to identify whether a candidate compound is a modulator of atherogenesis. In certain embodiments, the GPCR is human GPR84 which couples to the inhibitory Gi protein and is expressed endogenously in monocytes/macrophages. An agonist of GPR84 selectively modulates cytokine expression (interferon γ, tumor necrosis factor-α) in monocytes/macrophages, including decreasing monocyte chemoattractant protein-1 (MCP-1) expression. Agonists of the invention are useful as therapeutic agents for the prevention or treatment of atherosclerosis and atherosclerotic diseases, including coronary artery disease, myocardial infarction, peripheral arterial disease, and ischemic stroke. Agonists of the invention are addnl. useful as therapeutic agents for the prevention or treatment of conditions related to MCP-1 expression, including but not limited to rheumatoid arthritis, Crohn's disease, and multiple sclerosis.

CC **1-8** (Pharmacology)
Section cross-reference(s): 15.

ST G protein coupled receptor modulator **atherosclerosis** therapy; GPR84 receptor modulator **atherosclerosis** therapy; monocyte chemoattractant protein 1 modulator **atherosclerosis** therapy; MCP1 modulator **atherosclerosis** therapy

IT Transport proteins
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ABCA1 (ATP-binding cassette transporter subfamily A member 1); human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Fusion proteins (chimeric proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CTLA4-Ig, inhibitors, combination co-therapy with; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Inflammation
(Crohn's disease; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Intestine, disease
(Crohn's; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Nicotinic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR109A, agonists, combination co-therapy with; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

```
L7        25179 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ARTERY, DISEASE"/CT
L8        35151 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ATHEROSCLEROSIS/CT
L9        48956 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ATHEROSCLEROSIS/OBI OR
              ARTERIOSCLEROSIS/OBI
L10        9314 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ARTERIOSCLEROSIS/CT
L11       67514 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L7 OR L8 OR L9 OR L10)
L14        6717 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RESTENOSIS/OBI OR CORONARY
              RESTENOSIS/OBI
L15       68114 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 OR L14
L28             QUE  ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004 OR MY
              <2004 OR REVIEW/DT
L61        6519 SEA L6
L62          40 SEA L61 AND L15
L63          32 SEA L62 AND L28


=> dup rem l43 l63
FILE 'HCAPLUS' ENTERED AT 09:52:18 ON 06 JUN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'BIOSIS' ENTERED AT 09:52:18 ON 06 JUN 2007
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FILE 'EMBASE' ENTERED AT 09:52:18 ON 06 JUN 2007
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PROCESSING COMPLETED FOR L43
PROCESSING COMPLETED FOR L63
L76           57 DUP REM L43 L63 (1 DUPLICATE REMOVED)
                 ANSWERS '1-26' FROM FILE HCAPLUS
                 ANSWERS '27-44' FROM FILE BIOSIS
                 ANSWERS '45-57' FROM FILE EMBASE

=> d l76 1-26 ibib ed abs hitind

L76  ANSWER 1 OF 57  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:257391  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:288448
TITLE:                    Human G protein-coupled receptor GPR84 and modulators
                          thereof for treatment of atherosclerosis and
                          associated diseases and for treatment of conditions
                          related to MCP-1 expression
INVENTOR(S):              Hakak, Yaron; Unett, David J.; Gatlin, Joel; Liaw,
                          Chen W.
PATENT ASSIGNEE(S):       Arena Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 170pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2007027661         A2    20070308    WO 2006-US33651          20060829
     WO 2007027661         A3    20070426
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
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(GPR84 modulation of; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT G protein-coupled receptors
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GPR84; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Gi (adenylate cyclase-inhibiting), coupled with GPR84; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Neurotransmitter agonists
(adiponectin receptor 1 agonists, combination co-therapy with; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Neurotransmitter agonists
(adiponectin receptor 2 agonists, combination co-therapy with; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Inflammation
(allergic; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Antiarteriosclerotics
(antiatherosclerotics; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Bronchi, disease
(bronchiolitis obliterans syndrome; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Lung, disease
(chronic obstructive pulmonary disease; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Infection
(chronic viral hepatitis; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT HMG-CoA reductase inhibitors
(combination co-therapy with; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Blood coagulation disorders
(disseminated intravascular coagulation; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Nervous system, disease
(excitotoxic injury; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Liver, disease
(fatty; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Lung, disease
(fibrosis; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Allergy inhibitors
Alzheimer's disease
Anti-Alzheimer's agents
Anti-inflammatory agents
Anti-ischemic agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antifibrotic agents
Antihypertensives
Antiobesity agents
Antiosteoporotic agents
Antiparkinsonian agents
Antirheumatic agents
Asthma
Atherosclerosis
Cardiovascular agents
Cognitive disorders
Combination chemotherapy
Coronary artery disease
Coronary **restenosis**
Drug screening
Gastrointestinal agents
Gene therapy
Heart failure
Human
Hyperlipidemia
Hypertension
Hypolipemic agents
Ischemia
Macrophage
Molecular cloning
Monocyte
Mouse
Multiple sclerosis
Mus musculus
Myocardial infarction
Obesity
Osteoarthritis
Osteoporosis
Parkinson's disease
Prion diseases
Protein sequences
Psoriasis
Rat
Rattus norvegicus
Respiratory system agents

Rheumatoid arthritis
Transplant rejection
Vascular **restenosis**
cDNA sequences
(human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT G protein-coupled receptors
Monocyte chemoattractant protein-1
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Allergy
(inflammation; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Reperfusion
(injury; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Autoimmune disease
(insulin-dependent diabetes mellitus; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Diabetes mellitus
(insulin-dependent; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Inflammation
Kidney, disease
(interstitial nephritis; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Lung, disease
(interstitial; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Metabolic disorders
(metabolic syndrome X; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Diabetes mellitus
(non-insulin-dependent; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT **Artery, disease**
(peripheral; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proinflammatory, GPR84 modulation of; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis**

and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Arthritis
(psoriatic arthritis; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Fibrosis
(pulmonary; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Injury
(reperfusion; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Shock (circulatory collapse)
(septic; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Brain, disease
(stroke; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Lupus erythematosus
(systemic; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Inflammation
Intestine, disease
(ulcerative colitis; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Hepatitis
(viral, chronic; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, GPR84 modulation of; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 928180-03-4 928180-04-5
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(PCR primer; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 928180-18-1
RL: PRP (Properties)
(Unclaimed; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 928179-96-8D, G protein-coupled receptor GPR84 (human), subfragments are claimed 928179-98-0D, subfragments are claimed 928180-00-1D, subfragments are claimed 928180-02-3
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; human G protein-coupled receptor GPR84 and

modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 59-05-2, Methotrexate 550-24-3, 2,5-Dihydroxy-3-undecyl-1,4-benzoquinone 1191-85-1, 5,8,11,14-Eicosatetraynoic acid 927433-04-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination co-therapy with; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 9028-35-7 **9036-21-9**, PDE4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, combination co-therapy with; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 928179-95-7D, subfragments are claimed 928179-97-9D, subfragments are claimed 928179-99-1D, subfragments are claimed 928180-01-2
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 928180-19-2 928180-20-5 928180-22-7 928180-23-8 928180-24-9 928180-25-0 928180-26-1 928180-27-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 928180-21-6
RL: PRP (Properties)
(unclaimed protein sequence; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

IT 186144-43-4 186144-44-5 340774-93-8
RL: PRP (Properties)
(unclaimed sequence; human G protein-coupled receptor GPR84 and modulators thereof for treatment of **atherosclerosis** and associated diseases and for treatment of conditions related to MCP-1 expression)

L76 ANSWER 2 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:11040 HCAPLUS Full-text
DOCUMENT NUMBER: 146:93574
TITLE: Identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**
INVENTOR(S): Betz, Ulrich; D'Urso, Donatella; Gatsios, Petros; Seewald, Michael; Strayle, Jochen; Van Es, Helmuth Hendrikus Gerardus; Van Zutphen, Marlijn; Mesic, Emir

PATENT ASSIGNEE(S): Galapagos N. V., Belg.
SOURCE: PCT Int. Appl., 74pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007000292	A2	20070104	WO 2006-EP6117	20060624

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-695649P P 20050629
ED Entered STN: 04 Jan 2007

AB Methods of identifying proteins that may be used as targets for the treatment or prevention of cardiovascular disease, dyslipidemia, and atherosclerosis using the FlexSelect gene knock-in system are described. Genes and gene products may be targets drug therapy and methods of screening for drugs acting on these targets are described. The genes were identified in HepG2 cells using the level of secretion of apolipoprotein B100 as an indicator of a possible target. Screening for effectors of cysteinyl leukotriene receptor 2 and phosphodiesterase 4B is described.

CC **1-10** (Pharmacology)
Section cross-reference(s): 3

ST cardiovascular disease dyslipidemia **atherosclerosis** drug target gene knockin; screening cardiovascular hypolipemic agent antiatherosclerotic

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ADAMTS4; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ADORA1; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ADORA2A; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal

RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ADORA3; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(APEX1; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Adenosine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A2A, gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(BCKDK; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(BMP2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(CALCR; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(CEBPG; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DAPK2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DUSP4; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug**

screening)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(EDG4; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(EPHB1; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ESRRG; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(FGF1; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(FLJ10884; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(FZD1; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR100, gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(GPR100; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR101, gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias,

and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(GPR101; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(GPR109B; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(GPR10; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(GPR23; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HNF-4 (hepatocyte nuclear factor 4), gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(HSHNF4AGN; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(HTR2C; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IL22; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(INHBA; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ITLN2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MAP/microtubule affinity-regulating kinase 4 (MARK4), gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MAPK10; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MAPT; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MARK4; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MKNK2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MRGPRD; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MSP; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal

RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MVD; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Transcription factors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(NF-κB (nuclear factor of κ light chain gene enhancer in B-cells), genes regulated by, as drug targets; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Transcription factors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(NFAT (nuclear factor of activated T-cell), genes regulated by, as drug targets; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(NLK; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(NME3; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(NR2E1; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(OR1E2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(OSM; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(P2RY10; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug**

screening)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PCK2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PGK1, for use in treatment of cardiovascular disorders; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PHKG2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PLTP; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PRKCSH; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PRSS8; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PTGER2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PTGIR; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(RARA, for use in treatment of cardiovascular disorders; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(RIPK2; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(SERPINH1; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(SPPL3; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ST14; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(TEC; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(TNFRSF5; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(USP36; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Antiarteriosclerotics
(antiatherosclerotics, screening for; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Adeno-associated virus
Human herpesvirus
(as vector for delivery of therapeutic nucleic acids; identification of

targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Leukotriene receptors
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cysteine-containing LT-2, as drug target; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Orphan receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(estrogen-related receptor γ, gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Lentiviral vectors
(for delivery of therapeutic nucleic acids; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Antibodies and Immunoglobulins
Antisense DNA
Antisense RNA
Ribozymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for treatment and prevention of cardiovascular disease; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Gene, animal
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fosB, for use in treatment of cardiovascular disorders; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Bone morphogenetic protein 2
Calcitonin receptors
Prostacyclin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT Genetic methods
(gene knock-in; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Second messenger system
(genes regulated by, as drug targets; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT cDNA sequences
(identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT **Drug screening**
Drug targets
Human
(identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Reporter gene
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
(in **drug screening**; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microRNA, for treatment and prevention of cardiovascular disease; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Diagnosis
(mol.; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanobodies, for treatment and prevention of cardiovascular disease; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Cardiovascular agents
Hypolipemic agents
(screening for; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(short hairpin, for treatment and prevention of cardiovascular disease; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Double stranded RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small interfering, for treatment and prevention of cardiovascular disease; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT **Atherosclerosis**
Cardiovascular system, disease
Dyslipidemia
(treatment and prevention of; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP2, gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT **9036-21-9**, Phosphodiesterase 4B
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as drug target; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT 60-92-4, CAMP 7440-70-2, Calcium, biological studies 14127-61-8, Calcium dication, biological studies
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as second messenger, genes regulated by, as drug targets; identification of targets for treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis**)

IT 82391-38-6, Branched chain α-ketoacid dehydrogenase kinase 138069-86-0, APEX nuclease 241475-68-3, ADAMTS-1 306748-07-2, Dual specificity protein phosphatase 4

RL: BSU (Biological study, unclassified); BIOL (Biological study) (gene for; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

IT 391810-67-6

RL: ANT (Analyte); PRP (Properties); ANST (Analytical study) (nucleotide sequence; identification of drug targets for use in the treatment or prophylaxis of cardiovascular disorders, dyslipidemias, and **atherosclerosis** by gene knock-in and their use in **drug screening**)

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ACCESSION NUMBER: 2006:1010589 HCAPLUS Full-text

DOCUMENT NUMBER: 145:348598

TITLE: Methods and compositions using RP105 activators for the modulation of immune responses and autoimmune diseases

INVENTOR(S): Karp, Christopher L.; Divanovic, Senad

PATENT ASSIGNEE(S): Children's Hospital Medical Center, USA

SOURCE: PCT Int. Appl., 99pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-664001P P 20050322

ED Entered STN: 29 Sep 2006

AB The invention relates to regulation of inflammation and immune responses. The invention provides a method for treating a condition comprising administering a pharmaceutically effective amount of an activator of RP105. The condition is typically associated with TLR-4 activation and cytokine production Conditions addressed by the invention include sepsis, septic shock, inflammation, rheumatoid arthritis and Crohn's disease. The invention also provides the use of an activator of RP105 in the manufacture of a medicament for use in the treatment of a condition associated with cytokine production and methods for identifying an activator of RP105, which is also suitable for use in the treatment of a condition associated with stimulus-induced cytokine production More specifically, the invention relates to the use of RP105 as a specific inhibitor of TLR4 signaling and as a physiol. regulator of TLR4 signaling for the treatment of TLR4-mediated inflammation and immune-related diseases. The invention also relates to treating an animal having a disease or condition associated with toll-like receptor 4.

CC **1-7** (Pharmacology)
Section cross-reference(s): 63

IT Acne
Alzheimer's disease
Angiogenesis
Angiogenesis inhibitors
Anti-Alzheimer's agents
Anti-inflammatory agents
Anti-ischemic agents
Antiarthritics
Antiasthmatics
Anticoagulants
Antifibrotic agents
Antihypertensives
Antimalarials
Antiosteoporotic agents
Antioxidants
Antirheumatic agents
Antitumor agents
Antitussives
Antiulcer agents
Antiviral agents
Arthritis
Asthma
Atherosclerosis
Autoimmune disease
Bronchodilators
Cardiovascular agents
Celiac disease
Central nervous system, neoplasm
Combination chemotherapy
Common cold
Cough
Cystic fibrosis
Decongestants
Dendritic cell
Dopamine agonists
Drug delivery systems
Drug screening
Dyspnea
Emphysema
Encephalitis
Expectorants
Gastrointestinal agents
Gout
Gram-negative bacteria
Hepatitis virus
Herpesviridae
Human
Human herpesvirus
Human immunodeficiency virus
Hypercapnia
Hypoxia
Immune disease
Immunomodulators
Immunosuppressants
Inflammation
Lupus erythematosus
Macrophage
Malaria

Meningitis
Monocyte
Multiple organ failure
Multiple sclerosis
Nervous system agents
Osteoarthritis
Osteoporosis
Prophylaxis
Pruritus
Psoriasis
Rheumatoid arthritis
Sarcoidosis
Sepsis
Signal transduction, biological
Thrombosis
β2-Adrenoceptor agonists
(RP105 activators for modulation of immune responses and autoimmune diseases)

IT **Artery, disease**
(**restenosis**; RP105 activators for modulation of immune responses and autoimmune diseases)

IT 9001-84-7, Phospholipase A2 9001-87-0, Phospholipase D 9004-06-2, Elastase **9036-21-9**, Phosphodiesterase IV 80619-02-9, 5-Lipoxygenase 141907-41-7, Matrix metalloproteinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; RP105 activators for modulation of immune responses and autoimmune diseases)

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AB The present invention provides protein targets and methods for the screening for compds. useful in the prevention, amelioration or treatment of a cardiovascular disorder, dyslipidemia, and/or atherosclerosis. The invention also relates to the targets that were identified, especially G protein-coupled receptors, kinases, and proteases. Inhibiting target genes of the invention, or their expression products, by using compds. identifiable by methods of the invention, is beneficial in the treatment of diseases involving a cardiovascular disorder, dyslipidemia, and/or atherosclerosis. Addnl., mutations in genes encoding these proteins and alterations in levels of these proteins may be used in diagnosis of cardiovascular disorder, dyslipidemia, and/or atherosclerosis. Thus, adenoviral vectors encoding siRNAs were used in a high-throughput method to identify genes involved in ApoB100 secretion from HepG2 cells. A second assay used recombinant CHO-K1 cells expressing human cysteinyl leukotriene receptor 2 to screen for agonists/antagonists of this receptor. A cell-free assay using human phosphodiesterase 4B was also described.
CC **1-1** (Pharmacology)
Section cross-reference(s): 14
ST dyslipidemia **atherosclerosis** cardiovascular disease **drug screening**; diagnosis dyslipidemia **atherosclerosis** cardiovascular disease
IT Interleukins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (26; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)
IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)
IT Apolipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (A-V; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ABCA9 (ATP-binding cassette transporter subfamily A member 9); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ABCB7 (ATP-binding cassette transporter subfamily B member 7); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)
IT Cation channel
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ACCN5; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)
IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (AarF domain-containing kinase 1 (ADCK1); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AarF domain-containing kinase 2 (ADCK2); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BUB1 (budding uninhibited by benzimidazoles 1 homolog); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Nicotinic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CHRNA3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Cannabinoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CNR2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CRLF2 (cytokine receptor-like factor 2); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CRLR (calcitonin receptor-like receptor); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Chloride channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ClC-6; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DARC (Duffy antigen receptor for chemokines); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DOK-1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DP (docking protein); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DTDST (diastrophic dysplasia sulfate transporter); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Dlg5 (disks large 5); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D4; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ETL (EGF-TM7-latrophilin-related); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT EphA receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EphA4; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT EphB receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EphB6; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Fibroblast growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(FGFR4; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Growth factors, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(FIGF (c-fos-induced); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(FR-α (folate receptor α); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Frizzled-1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT GABA receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GABAA, GABRG3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPHA2 (glycoprotein hormone α2); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR126; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR148; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR15; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR21; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR22; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR32; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR40; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR48; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR65; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GPR78; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HECTD2 (HECT domain-containing 2); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HNF-4 (hepatocyte nuclear factor 4), HNF4G; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Histamine H2 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HRH4; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Interferon receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IFNAR1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Interleukin 12 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IL12RB2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Interleukin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IL22RA1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(KCTD7; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LG12 (leucine-rich repeat LGI family, member 2); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LRP6 (low-d. lipoprotein receptor-related protein 6); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MAP4K3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MASTL (microtubule-associated serine/threonine kinase-like); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Melanin-concentrating hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MCH-1R (melanin-concentrating hormone receptor 1); novel protein targets and
methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MPL (myeloproliferative leukemia virus oncogene); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MRGE (mas-related, G protein-coupled); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transcription factors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(NF-κB (nuclear factor of κ light chain gene enhancer in B-cells), promoter responsive to, in **drug screening**
; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transcription factors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(NFAT (nuclear factor of activated T-cell), promoter responsive to, in **drug screening**; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NIMA-related kinase 11 (NEK11); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Atrial natriuretic peptide receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NPR-C; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Nuclear receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NR0B2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Nuclear receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NR5A1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NSF (N-ethylmaleimide-sensitive factor); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ORL1 (opioid receptor-like 1); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PMS2L8 (postmeiotic segregation increased 2-like 8); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P2X; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P2Y; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RHAG (rhesus blood group-associated glycoprotein); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SAP102 (synapse-associated protein 102); novel protein targets and

methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SARA1 (SAR1a gene homolog 1); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SBREB3 (super-conserved receptor expressed in brain 3); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Sodium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SCN11A; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC17A5; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC22A2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC22A3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC22A4; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC28A2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC2A2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC6A11; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SLC9A7; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SPAP1 (SH2 domain-containing phosphatase anchor protein 1); novel protein

targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SRP72 (signal recognition particle 72 kDa); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SV2C (synaptic vesicle glycoprotein 2C); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TAP-1 (transporter in antigen processing 1); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Taste receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TAS1R3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Tumor necrosis factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TNFRSF10C and TNFRSF10D; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Cation channel
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TRPM6 (transient receptor potential cation channel subfamily M member 6); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Cation channel
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TRPM8; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (VN1R2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Vaccinia-related kinase 3 (VRK3); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (amino acid transporter SLC7A1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Antiarteriosclerotics
(antiatherosclerotics; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Angiogenic factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (brain specific angiogenesis inhibitor, BAI2; novel protein targets and

methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cAMP-, NF-κB-, or NF-AT-responsive, in **drug screening**; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Leukotriene receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cysteine-containing LT-2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Adenoviral vectors
Lentiviral vectors
Retroviral vectors
Viral vectors
(gene therapy with; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Diagnosis
(genetic; novel genes and proteins and methods of diagnosing cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hevin; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inward rectifier, Kir1.1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ionotropic, GRIN3B; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Diagnosis
(mol.; novel genes and proteins and methods of diagnosing cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT **Atherosclerosis**
Cardiovascular system, disease
Drug screening
Dyslipidemia
Human
(novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Angiotensin AT1 receptors
Calcitonin receptors
Melanocortin receptor 3
Progesterone receptors
β1-Adrenoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (retbindin; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Antibodies and Immunoglobulins
Antisense RNA
Antisense oligonucleotides
Ribozymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (screening for; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (short hairpin, screening for; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (sideroflexin, SRXN2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Double stranded RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (small interfering, screening for; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (transmembrane, TMEFF1 (transmembrane protein with EGF-like and two follistatin-like domains 1); novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study) (two pore domain, K2P5.1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Ryanodine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (type 1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (type 5-HT1F; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (type DP2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (type EP, PTGER4; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Growth inhibitors, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(vascular endothelial growth inhibitor; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Adeno-associated virus
Alphavirus
Human herpesvirus
Sendai virus
(vectors, gene therapy with; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(voltage-gated, KCND1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(voltage-gated, KCNF1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(voltage-gated, Kv7.3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(zinc finger-containing, ZFP91; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α7; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β2-; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(μ-opioid, μ1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9029-97-4, 3-Oxoacyl coenzyme A thiolase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ACAA2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 106640-75-9, Aldo-keto reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AKR1D1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and

atherosclerosis)

IT 37237-43-7, Glycoprotein galactosyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (B4GALT1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 366806-33-9, Casein kinase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CSNK2A1 and CSNK2B; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 62213-44-9, Dolichyl phosphate mannosyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (DPM1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 306298-47-5, Dual-specificity protein phosphatase 12
RL: BSU (Biological study, unclassified); BIOL (Biological study) (DUSP12; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9000-95-7, Ectonucleoside triphosphate diphosphohydrolase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ENTPD2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 149433-92-1, Eph kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (EPHA1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 149433-90-9, Elk kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (EPHB1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 68247-53-0, α-1,3-Fucosyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (FUT7; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 37257-19-5, Dihydroxyacetone phosphate acyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GNPAT; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 239106-98-0, Haspin
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GSG2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9028-41-5, Hydroxyacyl-coenzyme A dehydrogenase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HADH2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HDAC4; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and

atherosclerosis)

IT 9016-12-0, Hypoxanthine phosphoribosyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HPRT1; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 76901-02-5, 17-β-Hydroxysteroid dehydrogenase type 2
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HSD17B2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9044-85-3, Progesterone reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HSD3B7; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 219575-48-1, STE20-like kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (JIK; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9001-85-8, Lysophospholipase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (LYPLA3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9040-75-9, Monoglyceride lipase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MGLL; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9029-74-7, Nicotinamide N-methyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (NNMT; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT **9036-21-9**, Phosphodiesterase 4B
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PDE4B and PDE8A; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9068-52-4, Phosphodiesterase 6
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PDE6B; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9036-01-5, Phosphatidylinositol 4,5-bisphosphate 5-phosphatase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PIB5PA; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 115926-52-8, Phosphoinositide 3-kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PIK3R2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 104645-76-3, Phosphatidylinositol 4-phosphate 5-kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PIP5K1B; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and

atherosclerosis)

IT 362674-81-5, Protein phosphatase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PPP2R1B; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 361540-77-4, Protein phosphatase 3
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PPP3R2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 172522-01-9, AMP-activated protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PRKAG3; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 261955-11-7, Sentrin-specific proteinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SENP6; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 223484-06-8, Sphingosine-dependent protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SPHK2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9059-48-7, Sepiapterin reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SPR; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 86480-67-3, Ubiquitin carboxyl-terminal esterase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (UCHL1 and UCHL5; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9031-99-6, Dipeptidase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (isoform 2; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9000-81-1, Acetylcholinesterase 9001-80-3, Phosphofructokinase 9014-74-8, Enterokinase 9024-82-2, Phospholysine phosphohistidine inorganic pyrophosphate phosphatase 51901-16-7, 1-Acylglycerol-3-phosphate O-acyltransferase 76774-39-5, Ribonuclease L 79818-35-2, Lon proteinase 91608-96-7, Interferon-inducible double-stranded RNA-dependent protein kinase 142008-29-5, CAMP-dependent protein kinase 143180-74-9, Granzyme H 144697-16-5, BRAF kinase 146838-19-9, Tyrosine kinase ABL2 149146-91-8, NTRK2 receptor tyrosine kinase 153190-52-4, Gene PTK7 protein kinase 153967-26-1, Carboxypeptidase D 165245-96-5, Mitogen-activated protein kinase 14 169277-51-4, Gene c-mer protein kinase 174206-56-5, Protein kinase DYRK3 180189-96-2, Caspase 9 182372-11-8, Metalloproteinase ADAM12 189088-86-6, Protein kinase PAK3 189303-50-2, Cathepsin W 189460-40-0, Connective tissue growth factor 190606-18-9, MAP/microtubule affinity-regulating kinase 2 195127-66-3, Neurotrypsin 241824-56-6, Protein kinase DAPK2 245122-51-4, Proteinase inhibitor SPINK5 271597-13-8, Growth differentiation factor 10 284039-51-6, Serine/threonine kinase 22D 300830-60-8, Protein phosphatase PTPN9 300865-18-3, Receptor protein tyrosine phosphatase type M 301162-72-1, Protein tyrosine phosphatase PTPN3 330589-90-7,

Cytochrome P 450 2C19 342646-20-2, Protein phosphatase PTPN23 342900-44-1, Kallikrein 13 389069-73-2, Kallikrein 1 402476-24-8, Protein kinase CRK7 402736-19-0, Protein kinase SGK2 460720-13-2, Transmembrane serine protease 7 489461-60-1, Trypsin-2 676145-27-0, Protein phosphatase PTPN18 727737-71-5, Protein phosphatase PTPN21
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 140036-16-4, GENBANK M18391 201952-31-0, GenBank AF037333 321643-03-2, GenBank AF213045 321643-06-5, GenBank AF213050 382468-48-6, GenBank AF213048 392194-21-7, GENBANK D13814
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 60-92-4, CAMP
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(promoter responsive to, in **drug screening**; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 9014-00-0, Luciferase 9031-11-2, β-Galactosidase
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(reporter gene for, in **drug screening**; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 908612-06-6 908612-07-7 908612-08-8 908612-09-9 908612-10-2
908612-11-3 908612-12-4 908612-13-5 908612-14-6 908612-15-7
908612-16-8 908612-17-9 908612-18-0 908612-19-1 908612-20-4
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908614-36-8 908614-37-9 908614-38-0 908614-39-1 908614-40-4
908614-41-5

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(siRNA strand; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 908614-42-6 908614-43-7 908614-44-8 908614-45-9 908614-46-0
908614-47-1 908614-48-2 908614-49-3 908614-50-6 908614-51-7
908614-52-8 908614-53-9 908614-54-0

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(siRNA strand; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

IT 868829-11-2 908652-46-0 908652-47-1 908652-48-2 908652-49-3
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908652-55-1 908652-56-2 908652-57-3 908652-58-4 908652-59-5
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908652-75-5 908652-76-6 908652-77-7 908652-78-8 908652-79-9
908652-80-2 908652-81-3 908652-82-4 908652-83-5 908652-84-6
908652-85-7 908652-86-8 908652-87-9

RL: PRP (Properties)
(unclaimed sequence; novel protein targets and methods of screening for compds. useful in treatment of cardiovascular disorders, dyslipidemia and **atherosclerosis**)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 5 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:982167 HCAPLUS Full-text
DOCUMENT NUMBER: 145:348597
TITLE: Use of phenylmethimazoles, methimazole derivatives, and tautomeric cyclic thiones for the treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression
INVENTOR(S): Kohn, Leonard D.; Harii, Norikazu; Benavides-Peralta, Uruguaysito; Gonzalez-Murguiondo, Mariana; Lewis, Christopher J.; Napolitano, Giorgio; Giuliani, Cesidio; Malgor, Ramiro; Goetz, Douglas J.
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 102 pp., Cont.-in-part of U.S. Ser. No. 912,948.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006211752	A1	20060921	US 2005-130922	20050517
US 2005209295	A1	20050922	US 2004-801986	20040316
AU 2004317993	A1	20051013	AU 2004-317993	20040316
CA 2559712	A1	20051013	CA 2004-2559712	20040316
EP 1725230	A1	20061129	EP 2004-821836	20040316
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 2006058365	A1	20060316	US 2004-912948	20040806
WO 2006124676	A1	20061123	WO 2006-US18554	20060511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.:

US 2004-801986	A2 20040316
US 2004-912948	A2 20040806
WO 2004-US7888	A 20040316
US 2005-130922	A 20050517

OTHER SOURCE(S): MARPAT 145:348597
ED Entered STN: 22 Sep 2006
AB The present invention relates to the treatment of autoimmune and/or inflammatory diseases associated with overexpression of Toll-like receptor 3 (TLR3) as well as Toll-like receptor 4 (TLR4) and/or TLR3/TLR4 signaling in nonimmune cells, monocytes, macrophages, and/or dendritic cells in association with related pathologies. This invention also relates to the use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for the treatment of autoimmune and inflammatory diseases associated with Toll-like receptor 3 (TLR3) as well as Toll-like receptor 4 (TLR4) and/or TLR3/TLR4 signaling in nonimmune cells, monocytes, macrophages, and/or dendritic cells in association with related pathologies. This invention also relates to treating a subject having a disease or condition associated with abnormal Toll-like receptor 3 as well as Toll-like receptor 4 and/or TLR3/TLR4 signaling in nonimmune cells, monocytes, macrophages, and/or dendritic cells in association with related pathologies. The present invention also relates to the treatment of autoimmune-inflammatory pathologies and chemokine and cytokine-mediated diseases associated with TLR overexpression and signaling. This invention also relates to pharmaceutical formulations capable of inhibiting the IRF-3/Type 1 IFN/STAT/ISRE/IRF-1 pathway associated with Toll-like receptor overexpression or signaling.
INCL 514389000
CC **1-7** (Pharmacology)
Section cross-reference(s): 9
IT **Artery, disease**

Inflammation
(arteritis, temporal; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT Angioplasty
Transplant and Transplantation
(**atherosclerosis** from; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT **Artery, disease**
(coronary, stenosis, calcific, acute-phase response in; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT **Artery, disease**
(coronary; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT **Artery, disease**
(intima, hyperplasia, coronary, following angiograph; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT **Artery, disease**
Inflammation
(periarteritis nodosa; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT **Artery, disease**
(**restenosis**; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT Medical goods
(stents, **atherosclerosis** from; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT Vein
(transplant, **atherosclerosis** from; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT AIDS (disease)
Acute-phase response
Addison's disease
Alopecia
Animal cell
Anti-inflammatory agents
Anti-ischemic agents
Antiarthritics
Antiasthmatics
Antibacterial agents
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antifibrotic agents
Antihypertensives
Antimalarials
Antiphospholipid syndrome

Antirheumatic agents
Antitumor agents
Arthritis
Asthma
Atherosclerosis
Autoimmune disease
Behcet's syndrome
Blood vessel, disease
Cachexia
Calcium channel blockers
Cardiovascular agents
Cardiovascular system, disease
Chronic lymphocytic leukemia
Combination chemotherapy
Dendritic cell
Dermatitis
Dermatomyositis
Diabetes mellitus
Diagnosis
Drug delivery systems
Drug screening
Dyslipidemia
Dyspnea
Emphysema
Endotoxemia
Fibrosis
Food allergy
Granulomatous disease
Graves' disease
Hodgkin's disease
Human
Hypercholesterolemia
Hyperglycemia
Hyperlipidemia
Hypertension
Hypertriglyceridemia
Hypolipemic agents
Hypothyroidism
Inflammation
Ischemia
Macrophage
Malaria
Melanoma
Metabolic disorders
Monocyte
Multiple myeloma
Multiple sclerosis
Myasthenia gravis
Myeloid leukemia
Neoplasm
Osteoarthritis
Platelet aggregation
Platelet aggregation inhibitors
Prognosis
Prophylaxis
Pruritus
Psoriasis
Rheumatic fever
Rheumatoid arthritis
Septicemia

Signal transduction, biological
Sjogren syndrome
Thrombosis
Tooth
Transplant rejection
Vitiligo
(use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT Transplant and Transplantation
(vein, **atherosclerosis** from; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

IT 9000-92-4, Amylase 9001-42-7, α-Glucosidase 9001-62-1, Lipase 9001-87-0, Phospholipase D 9004-02-8, Lipoprotein lipase 9004-06-2, Elastase 9015-82-1 9027-63-8, ACAT 9027-95-6, ATP-citrate lyase 9028-31-3, Aldose reductase 9028-35-7, HMG-CoA reductase 9028-93-7, IMP dehydrogenase 9029-62-3, Squalene epoxidase 9035-74-9, Glycogen phosphorylase **9036-21-9**, PDE4 9040-59-9, Cyclic nucleotide phosphodiesterase 9077-14-9, Squalene synthetase 39391-18-9, Cyclooxygenase 54249-88-6, Dipeptidyl peptidase IV 67340-07-2, Acyl-CoA carboxylase 80619-02-9, 5-Lipoxygenase 90119-07-6, LTA4 hydrolase 133876-97-8, Phospholipase A2 165245-96-5, p38 Mitogen-activated protein kinase 300865-11-6, Protein tyrosine phosphatase 1B 329900-75-6, Cyclooxygenase 2 329967-85-3, Cyclooxygenase 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, co-treatment with; use of phenylmethimazoles, methimazole derivs., and tautomeric cyclic thiones for treatment of autoimmune/inflammatory diseases associated with toll-like receptor overexpression)

L76 ANSWER 6 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1241075 HCAPLUS Full-text
DOCUMENT NUMBER: 144:5408
TITLE: Targeting RP105 for the modulation of immune responses and autoimmune diseases
INVENTOR(S): Karp, Christopher L.; Divanoic, Senad
PATENT ASSIGNEE(S): Children's Hospital Medical Center, USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110470	A2	20051124	WO 2005-US12931	20050414
WO 2005110470	A3	20060803		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-562794P P 20040416
US 2005-664001P P 20050322

ED Entered STN: 24 Nov 2005

AB The authors disclose the use of an activator of RP105 (CD180 antigen) in the manufacture of a medicament for use in the treatment of a condition associated with cytokine production and methods for identifying an activator of RP105, which is also suitable for use in the treatment of a condition associated with stimulus-induced cytokine production In one example, RP105, in conjunction with MD-1, specifically inhibited Toll-like receptor 4 signaling and subsequent production of interleukin-8.

IC ICM A61K039-00

CC 15-10 (Immunochemistry)
Section cross-reference(s): **1**, 2, 14

IT **Drug screening**
(for activators of RP105)

IT **Artery, disease**
(**restenosis**; targeting RP105 for modulation of immune responses and autoimmune diseases)

IT Acne
Alzheimer's disease
Arthritis
Asthma
Atherosclerosis
Burn
Celiac disease
Central nervous system, neoplasm
Common cold
Cough
Cystic fibrosis
Dyspnea
Emphysema
Encephalitis
Gout
Human
Hypercapnia
Hyperoxia
Hypertension
Hypoxia
Lupus erythematosus
Malaria
Meningitis
Multiple organ failure
Multiple sclerosis
Osteoarthritis
Osteoporosis
Pruritus
Psoriasis
Sarcoidosis
Thrombosis
(targeting RP105 for modulation of immune responses and autoimmune diseases)

IT 9001-84-7, Phospholipase A2 9001-87-0, Phospholipase D 9004-06-2, Elastase **9036-21-9**, Cyclic nucleotide phosphodiesterase 71160-24-2, LTB4 141907-41-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; in therapeutic combination with activators of RP105)

L76 ANSWER 7 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:523313 HCAPLUS Full-text
DOCUMENT NUMBER: 143:38415
TITLE: Biomarkers for the efficacy of calcitonin and parathyroid hormone analog **treatment**
INVENTOR(S): Bobadilla, Maria
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005053731	A1	20050616	WO 2004-EP13347		20041124 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004294268	A1	20050616	AU 2004-294268		20041124 <--
CA 2546111	A1	20050616	CA 2004-2546111		20041124 <--
EP 1689427	A1	20060816	EP 2004-819617		20041124 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
CN 1905894	A	20070131	CN 2004-80040915		20041124 <--
BR 2004016945	A	20070213	BR 2004-16945		20041124 <--
US 2007099828	A1	20070503	US 2006-580779		20060525 <--
PRIORITY APPLN. INFO.:			US 2003-525025P	P	20031125 <--
			WO 2004-EP13347	W	20041124

ED Entered STN: 17 Jun 2005

AB Gene expression assays were performed using tissues of monkeys treated with the calcitonin or parathyroid hormone analog (e.g., PTS 893) at sub-therapeutic dose. The assays were analyzed to identify the modes of actions of calcitonin or parathyroid hormone with relationships to therapeutic applications. Among the biomarkers are the expression profiles of the genes for Y-box binding protein, bone morphogenetic proteins, fibroblast growth factors, insulin-like growth factors, vascular endothelial growth factor, α-2-HS glycoprotein, osteoclast stimulating factor, nuclear receptors (steroid/thyroid family), and others. The results obtained support the anabolic effect of salmon calcitonin on bone metabolism

IC ICM A61K038-23
ICS A61K038-29; A61P019-08; C12Q001-68
CC **1-10** (Pharmacology)
ST gene expression profile calcitonin and parathyroid hormone analog efficacy; growth regulator disease **drug screening** gene expression profile
IT Cyclins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(A2; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)
IT Fetuins

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(A; biomarkers for determining efficacy of calcitonin and parathyroid hormone
analog **treatment** for disorders of growth regulators)

IT DNA microarray technology
Gene expression profiles, animal
(Affymetrix HG-U95A2 GeneChip; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Cyclins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(B1; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Bone morphogenetic protein 2
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(BMP-2A; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(COMP (cartilage oligomeric matrix protein); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(CREM (cAMP-responsive element modulator); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Calcium-binding proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(CaBP1; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Cyclins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(D2; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(DMP1; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Cyclins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(E2; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT G protein-coupled receptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(EDG-6 (endothelial differentiation gene 6); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(GADD45; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(GRB-10 (growth factor receptor-bound protein 10); biomarkers for determining
efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Heat-shock proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(HSP 47; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Insulin-like growth factor-binding proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(IGFBP-2; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Insulin-like growth factor-binding proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(IGFBP-3; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Insulin-like growth factor-binding proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(IGFBP-5; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(IκB-α (NF-κB **inhibitor** α); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(JIP-1 (c-Jun N-terminal kinase-interacting protein-1); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(LIM domain-containing; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(MAGUK (membrane-associated guanylate kinase); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(MMD (mitogen-to-macrophage differentiation-associated); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(Miz-1 (Msx-interacting-zinc finger); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(NFAT (nuclear factor of activated T-cell); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(OS4; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(PC-1; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(PDGF-associated; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(PIG-G (phosphatidylinositol glycan class G); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(PIG-L (phosphatidylinositol glycan class L); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(PRKCSH (protein kinase C substrate 80K-H); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Purinoceptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(P2Y; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(RUNX2 (runt-related transcription factor 2); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Retinoid X receptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(RXRγ; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT G proteins (guanine nucleotide-binding proteins)
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(Rac2; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(SCAMP1 (secretory carrier membrane protein 1); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(SF-1 (steroidogenic factor 1); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(STAT1 (signal transducer and activator of transcription 1); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(STAT2 (signal transducer and activator of transcription 2); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(STAT5A (signal transducer and activator of transcription 5A);

biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(STAT5B (signal transducer and activator of transcription 5B); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(STAT6 (signal transducer and activator of transcription 6); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(Smad-3; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(Smad-5; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(Smad-6; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(TEIG (transforming growth factor β-inducible early growth response); biomarkers for determining efficacy of calcitonin and parathyroid
hormone analog **treatment** for disorders of growth regulators)

IT Transforming growth factor receptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(TGF-β receptor, type III; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(TIEG (transforming growth factor β-induced anti-apoptotic factor 1); biomarkers for determining efficacy of calcitonin and parathyroid
hormone
analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(TRIO (triple functional domain); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(Tob; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Annexins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(V; biomarkers for determining efficacy of calcitonin and parathyroid
hormone
analog **treatment** for disorders of growth regulators)

IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(YB-1 (Y box-binding, 1); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of

growth regulators)
IT Activin receptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(activin A type II-like 1; biomarkers for determining efficacy of calcitonin
and parathyroid hormone analog **treatment** for disorders of growth regulators)
IT Antiarteriosclerotics
(antiatherosclerotics; biomarkers for determining efficacy of calcitonin and
parathyroid hormone analog **treatment** for disorders of growth regulators)
IT Anabolic agents
Biomarkers
Drug screening
Human
Macaca irus
Mammalia
Nucleic acid amplification (method)
Nucleic acid hybridization
Primates
Test kits
(biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)
IT Primers (nucleic acid)
Probes (nucleic acid)
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)
IT Amelogenins
Biglycans
Bone morphogenetic protein 1
Bone morphogenetic protein 10
Bone morphogenetic protein 5
Bone morphogenetic protein 6
Calreticulin
Estrogen receptors
Fibroblast growth factor receptors
Insulin-like growth factor-binding proteins
Osteopontin
Proliferating cell nuclear antigen
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)
IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(estrogen receptor-related; biomarkers for determining efficacy of calcitonin
and parathyroid hormone analog **treatment** for disorders of growth regulators)
IT Transcription factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(estrogen-responsive B box; biomarkers for determining efficacy of calcitonin
and parathyroid hormone analog **treatment** for disorders of growth regulators)
IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(follistatin-like 1; biomarkers for determining efficacy of calcitonin and

parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(lysyl oxidase-like; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Glutamate receptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(metabotropic, mGluR1; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteoglycans, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(neurocan; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(neurochondrin; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Cyclin dependent kinase **inhibitors**
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(p21CIP1; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteoglycans, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(perlecans; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transport proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(phosphatidylinositol transfer protein; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transport proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(proton pump; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(transforming growth factor β-induced apoptosis protein 12; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT **Atherosclerosis**
(**treatment** of; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Inositol 1,4,5-trisphosphate receptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type 1; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Inositol 1,4,5-trisphosphate receptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type 2; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type I, fusion protein with platelet-derived growth factor B; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type I, α2-subunit; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type II, α1-subunit; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Activin receptors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type IIB; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type III, α1-subunit; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type IV, α2-subunit; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type IX, α1-subunit; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type VI, α1 and α2-subunit; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type XI, α1 and α2-subunit; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Collagens, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type XVI, α1-subunit; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Enzymes, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(ubiquitin-conjugating; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Proteoglycans, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(versicans; biomarkers for determining efficacy of calcitonin and parathyroid

hormone analog **treatment** for disorders of growth regulators)

IT Tubulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(α-, isotype H2; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Integrins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(α10; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Tubulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(α1-; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Globulins, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(α2-PEG (α2-pregnancy-associated endometrial globulin); biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Tubulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(α3-; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Platelet-derived growth factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(β, fusion protein with collagen type I; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Tubulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(β-, cofactor D; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transforming growth factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(β-; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Transforming growth factors
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(β3-; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Tubulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(β2-; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Tubulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(β3-; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT Tubulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(β4-; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 113356-28-8, Inositol 1(4) phosphatase
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(1 and 2; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 9001-77-8

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(1, isoform a; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 9035-54-5, Chorionic somatomammotropin 142805-58-1
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(1; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT **9036-21-9**, Phosphodiesterase 4A
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(4A and 4D and E3 abnd IB; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 9016-17-5
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(E; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 9001-03-0
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(I and II; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 9001-87-0, Phospholipase D 9025-32-5, Prolidase 9026-43-1 9028-06-2, Proline 4-hydroxylase 9059-25-0, Collagen lysine hydroxylase 37205-54-2, Phosphatidylinositol 4-kinase 62046-94-0, Somatomedin A 63551-76-8, Phospholipase Cβ3 64060-24-8, Osteoclast activating factor 67763-97-7, IGF-2 81669-70-7 83869-56-1, GM-CSF 90698-26-3, Ribosomal protein S6 kinase 94716-09-3, Cathepsin K 99194-04-4, Cystatin B 106096-92-8 106283-10-7, Inositol 1,4,5-trisphosphate 3-kinase 115926-52-8, Phosphoinositide 3 kinase 119699-77-3, Inositol polyphosphate 5-phosphatase 123584-45-2, Fibroblast growth factor 4 127464-60-2, Vascular endothelial growth factor 137632-08-7, Mitogen-activated protein kinase 1 141436-78-4, Protein kinase Cα 142008-29-5, CAMP-dependent protein kinase 142441-65-4, Caldecrin 144388-35-2, UDP-acetylglucosamine-phosphatidylinositol α1,6-Acetylglucosaminyltransferase 146702-84-3, Mitogen-activated protein kinase kinase kinase 1 146838-21-3, Gene SNF1 protein kinase 146838-30-4, Mitogen-activated protein kinase-activated protein kinase 2 147014-96-8, Cyclin-dependent kinase 5 147171-38-8, CDC like kinase 1 151662-20-3, Myotonic dystrophy protein kinase 157482-36-5, Janus kinase 3 161108-11-8, Serine proteinase 11 162032-63-5, DDR Receptor tyrosine kinase 167397-96-8, Interleukin 1 receptor-associated kinase 169150-71-4 172306-41-1, Protein kinase PCTAIRE1 175449-82-8, Collagenase 3 175780-17-3, Mitogen-activated protein kinase-activated protein kinase 3 189303-50-2, Cathepsin W 189460-40-0, Connective tissue growth factor 190606-22-5, Protein kinase 38 192333-55-4, MAPK13 192662-83-2, Vascular endothelial growth factor B 212625-17-7, Ste20 related kinase SPAK 220064-77-7, PAK4 kinase 220324-84-5, Clk2 kinase 252901-98-7, Tousled like kinase 1 289898-51-7, Mitogen-activated protein kinase 8 303014-92-8, Cyclin-dependent kinase 6 306298-57-7, Dual specificity protein phosphatase 9 322637-18-3, Fibroblast growth factor 18 333425-95-9, Protein kinase D2 352031-63-1, Fibroblast activation protein α 370088-29-2, Mitogen-activated protein kinase kinase kinase kinase 4 386278-22-4, Death associated protein kinase 3
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 9002-64-6, Parathyroid hormone 9002-64-6D, Parathyroid hormone, analogs 9007-12-9, Calcitonin 47931-85-1, Salmon calcitonin 155383-07-6, SDZ PTS 893
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 372092-80-3, Protein kinase
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(cytokine-inducible; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 104645-76-3, Phosphatidylinositol 4-phosphate 5-kinase
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(isoform C and type Iβ and type II; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 140879-24-9, Proteasome
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(subunit β10; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 7440-70-2, Calcium, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**treatment** of disorders of metabolism of; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 111693-80-2, Inositol polyphosphate 4-phosphatase
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(type Iβ; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 9000-83-3, ATPase
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(vacuolar; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 114949-22-3, Activin
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(β, C chain; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

IT 475489-73-7, Calcium/calmodulin-dependent kinase II
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(γ; biomarkers for determining efficacy of calcitonin and parathyroid hormone analog **treatment** for disorders of growth regulators)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 8 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1059165 HCAPLUS Full-text
DOCUMENT NUMBER: 142:721
TITLE: Treatment of cardiovascular pathology with PDE4 inhibitors
INVENTOR(S): Barone, Frank C.; Coatney, Robert W.; Legos, Jeffrey J.
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004105751	A1	20041209	WO 2004-US16720	20040527 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-473728P P 20030528 <--
ED Entered STN: 10 Dec 2004
AB The invention relates to a method of reducing cardiovascular pathol. in a mammal using an inhibitors of phosphodiesterase 4 (PDE4).
IC ICM A61K031-40
CC **1-8** (Pharmacology)
IT Antihypertensives
Atherosclerosis
Cardiovascular system, disease
Hypertension
(treatment of cardiovascular pathol. with PDE4 inhibitors)
IT **9036-21-9, Phosphodiesterase 4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; treatment of cardiovascular pathol. with PDE4 inhibitors)
IT 61413-54-5, Rolipram 162401-32-3, Roflumilast
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treatment of cardiovascular pathol. with PDE4 inhibitors)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 9 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:965396 HCAPLUS Full-text
DOCUMENT NUMBER: 141:391042
TITLE: Crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**
INVENTOR(S): Brown, David Graham; Groom, Colin Roger; Hopkins, Andrew Lee; Jenkins, Timothy Mark; Kamp, Sarah Helen; O'Gara, Margaret Mary; Ringrose, Heather Joan; Robinson, Colin Mark; Taylor, Wendy Elaine
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 250 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004097010	A1	20041111	WO 2004-IB1332	20040421 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2522472	A1	20041111	CA 2004-2522472	20040421 <--
EP 1623026	A1	20060208	EP 2004-728609	20040421 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004009931	A	20060425	BR 2004-9931	20040421 <--
JP 2006525801	T	20061116	JP 2006-506553	20040421 <--
PRIORITY APPLN. INFO.:			GB 2003-10058 A	20030501 <--
			WO 2004-IB1332 W	20040421

ED Entered STN: 12 Nov 2004

AB The present invention relates to the soakable crystals of a phosphodiesterase 5 (PDE5) and their uses in identifying PDE5 ligands, including PDE5 ligands and inhibitor compds. The present invention also relates to methods of identifying such PDE5 inhibitor compds. and their medical use. The present invention addnl. relates to crystals of PDE5 into which ligands may be soaked and crystals of PDE5 10 comprising PDE5 ligands that have been soaked into the crystal.

IC ICM C12N009-16
ICS A61K031-00; G01N033-68

CC 7-5 (Enzymes)
Section cross-reference(s): **1**, 75

ST human phosphodiesterase 5 Sildenafil complex crystal structure sequence; drug design human phosphodiesterase 5 **inhibitor**; engineering mutagenesis design human phosphodiesterase 5

IT Blood vessel, disease
(Kawasaki; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Cryoprotectants
(PDE5 stabilization solution comprising; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Carbohydrates, uses
RL: NUU (Other use, unclassified); USES (Uses)
(PDE5 stabilization solution comprising; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Enzyme functional sites
(active; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Allergy
(allergic asthma; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Allergy
Inflammation
Nose, disease
(allergic rhinitis; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Asthma

(allergic; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Heart, disease
(angina pectoris, stable, unstable and variant Prinzmetal; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Intestine
(anus, fissure; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Sexual disorders
(arousal, female, orgasmal; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Autonomic nervous system, disease
(autonomic neuropathy; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Prostate gland, disease
(benign hyperplasia; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Hyperplasia
(benign prostatic; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Bronchi, disease
Inflammation
(bronchitis; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Crystal growth
(by vapor diffusion, hanging drop vapor diffusion, macro or micro-seeding, sitting drop vapor diffusion; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Lung, disease
(chronic obstructive pulmonary disease; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Asthma
(chronic; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Reproductive system
(clitoris, dysfunction; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT **Artery, disease**
(coronary; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Allergy **inhibitors**
Alopecia
Alzheimer's disease
Anti-Alzheimer's agents
Antiarteriosclerotics
Antiasthmatics
Antidiabetic agents
Antiglaucoma agents
Antihypertensives
Antitumor agents
Arteriosclerosis
Blood vessel, disease
Conformation

Crystal structure
Diabetes mellitus
Disease, animal
Drug delivery systems
Drug design
Drug screening
Eye, disease
Glaucoma (disease)
Human
Hypertension
Mammalia
Molecular modeling
Multiple sclerosis
Neoplasm
Preeclampsia
Protein engineering
Protein motifs
Psoriasis
Respiratory failure
(crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Ligands
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Polyoxyalkylenes, uses
RL: NUU (Other use, unclassified); USES (Uses)
(crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Crystallization
(del; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Kidney, disease
(diabetic nephropathy; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Nerve, disease
(diabetic neuropathy; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Menstrual disorder
(dysmenorrhea; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Temperature
pH
(effects of crystallzation; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Blood pressure
(elevated intra-ocular; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Heart, disease
(failure; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(for crystallzation; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT Stomach, disease
(gastroparesis; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Dialysis
(hemodialysis, stabilization of blood pressure during; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Vein, disease
(hemorrhoid; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Vasoconstriction
(hypoxic; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Sexual disorders
(impotence; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Bladder, disease
(incontinence; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT 5-HT reuptake **inhibitors**
(induced sexual dysfunction; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Spinal cord, disease
(injury, sexual disorder due to; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Intestine, disease
(irritable bowel syndrome; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Conformation
(loop, protein, of PDE5; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Eye, disease
(macula, degeneration; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Neoplasm
(metastasis; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Crystallization
(microcrystn.; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Skin, disease
(necrosis; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Nerve, disease
(neuropathy, eye; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Nerve, disease
(neuropathy; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Esophagus
(nutcracker; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Bladder, disease
(obstruction; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT **Artery, disease**
(occlusion; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Blood vessel, disease
(peripheral; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(phosphodiesterase 4 loop with phosphodiesterase 5 in; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Angioplasty
(post percutaneous transluminal coronary; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Parturition disorders
(premature parturition; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Hypertension
(pulmonary; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Eye
(retina, occlusion; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Mutagenesis
(site-directed; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Necrosis
(skin; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Dialysis
(soakable crystals grown by; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Injury
(spinal cord, sexual disorder due to; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT Brain, disease
(stroke; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT 14797-55-8, Nitrate, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-induced tolerance; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT 67-68-5, DMSO, uses
RL: NUU (Other use, unclassified); USES (Uses)
(PDE5 ligands in; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT 50-70-4, Sorbitol, uses 56-81-5, Glycerol, uses 87-99-0, Xylitol 107-41-5, 2-Methyl-2,4-pentanediol
RL: NUU (Other use, unclassified); USES (Uses)
(PDE5 stabilization solution comprising; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)
IT 787859-38-5 787859-39-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study)
(amino acid sequence; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**
)

IT 7365-45-9, HEPES
RL: NUU (Other use, unclassified); USES (Uses)
(buffer, for crystallzation; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT **9036-21-9D**, Phosphodiesterase 4, loop region fusion protein with PDE5
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 212432-75-2, GENBANK AB001635
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 9068-52-4D, Phosphodiesterase 5, and Sildenafil complex
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 139755-83-2D, Sildenafil, phosphodiesterase 5 complex
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 67-63-0, Isopropanol, uses 25322-68-3, PEG 4000
RL: NUU (Other use, unclassified); USES (Uses)
(for crystallzation; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**
)

IT 521942-16-5
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 loop region sequence; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 139756-21-1, 5-(2-Ethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one 190281-17-5, Pyrazolopyrimidinone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphodiesterase 5 active site accommodating; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 521942-15-4
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(phosphodiesterase 5 loop region sequence; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 9004-10-8, Insulin, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(resistance; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 787860-70-2 787860-71-3 787860-72-4 787860-73-5 787860-74-6 787860-75-7 787860-76-8 787860-77-9
RL: PRP (Properties)

(unclaimed nucleotide sequence; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

IT 787860-68-8 787860-69-9
RL: PRP (Properties)
(unclaimed protein sequence; crystal structures of human phosphodiesterase 5 and its ligand complex and their use in screening for **inhibitor**)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 10 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:965063 HCAPLUS Full-text
DOCUMENT NUMBER: 141:410960
TITLE: Preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors
INVENTOR(S): Dube, Daniel; Dube, Laurence; Gallant, Michel; Lacombe, Patrick; Deschenes, Denis; MacDonald, Dwight
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004096220	A1	20041111	WO 2004-CA622		20040427 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004234190	A1	20041111	AU 2004-234190		20040427 <--
CA 2523336	A1	20041111	CA 2004-2523336		20040427 <--
EP 1635829	A1	20060322	EP 2004-729586		20040427 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
CN 1812787	A	20060802	CN 2004-80018346		20040427 <--
JP 2006524638	T	20061102	JP 2006-504121		20040427 <--
US 2006223850	A1	20061005	US 2005-554176		20051021 <--
PRIORITY APPLN. INFO.:			US 2003-466542P	P	20030430 <--
			WO 2004-CA622	W	20040427

OTHER SOURCE(S): MARPAT 141:410960
ED Entered STN: 12 Nov 2004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title 8-phenylquinolines I [S1-S3 = H, OH, halo, alkyl, etc.; R1 = CO2aryl, CONHaryl, CONHheteroaryl, etc.; Ar1, Ar2 = (hetero)aryl or an N-oxide thereof; R2 = H, aryl, haloaryl, heterocyclyl, etc.; R3 = H, alkyl, hydroxyalkyl, etc.; R4 = H, halo, CN, alkyl, etc.] which are PDE4 inhibitors, were prepared E.g., a multi-step synthesis of II (no characterization data given for intermediates), which showed IC50 of 0.155 μM in LPS and FMLP-induced TNF-α and LTB4 assays in human whole blood, was given. The pharmaceutical compns. comprising the compound I are claimed.

IC ICM A61K031-4709
ICS C07D417-10; C07D417-14; C07D471-04; A61P029-00; C07D413-10; C07D401-10; C07D401-14; C07D409-10; C07D215-14; C07D413-14; C07D513-04; C07D215-12

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**, 63

IT Inflammation
(Crohn's disease, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Intestine, disease
(Crohn's, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Antihistamines
(H1, co-drugs; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors for use in combination with other therapeutic agents)

IT Muscarinic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(M2, M2/M3 antagonists as co-drugs; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors for use in combination with other therapeutic agents)

IT Muscarinic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(M3, M2/M3 antagonists as co-drugs; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors for use in combination with other therapeutic agents)

IT Respiratory distress syndrome
(adult, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Allergy
Inflammation
Nose, disease
(allergic rhinitis, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Inflammation
Spinal column, disease
(ankylosing spondylitis, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Dermatitis

(atopic, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Bronchi, disease
Inflammation
(chronic bronchitis, treating; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Lung, disease
(chronic obstructive pulmonary disease, treating; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Leukotriene antagonists
β2-Adrenoceptor agonists
(co-drugs; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors for use in combination with other therapeutic agents)

IT Corticosteroids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(co-drugs; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors for use in combination with other therapeutic agents)

IT Abdomen, disease
(colic, treating or preventing laminitis or colic in horses; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Eye, disease
Inflammation
(conjunctivitis, treating or preventing vernal conjunctivitis; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Mental and behavioral disorders
(depression, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Granuloma
(eosinophilic, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Inflammation
Kidney, disease
(glomerulonephritis, treating or preventing chronic glomerulonephritis; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Transplant and Transplantation
(graft-vs.-host reaction, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Injury
(head and neck, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Reperfusion
(injury, treating or preventing reperfusion injury of the brain; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Head and Neck, disease
(injury, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Hoof, disease
Inflammation

(laminitis, treating or preventing laminitis or colic in horses; preparation
of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Leukotrienes
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene biosynthesis inhibitors as co-drugs; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors for use in combination with other therapeutic agents)

IT Inflammation
(neurogenic, treating or preventing neurogenic inflammation; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Respiratory distress syndrome
(newborn, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Anti-inflammatory agents
(nonsteroidal; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Allergy inhibitors
Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidepressants
Antiparkinsonian agents
Antirheumatic agents
Antitumor agents
Antitussives
Cognition enhancers
Human
Immunosuppressants
(preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Skin, disease
(proliferative, treating or preventing benign or malignant proliferative skin diseases; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Arthritis
(psoriatic arthritis, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Injury
(reperfusion, treating or preventing reperfusion injury of the brain; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT **Artery, disease**
(**restenosis**, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Gastric acid
(secretion, treating or preventing hypersecretion of gastric acid; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Shock (circulatory collapse)
(septic, treating or preventing bacterial, fungal or viral induced septic shock; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT Proteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(statin, co-drugs; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors for use in combination with other therapeutic agents)
IT Spinal cord, disease
(trauma, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT Multiple sclerosis
(treating or preventing acute and chronic multiple sclerosis; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT Sepsis
(treating or preventing bacterial, fungal or viral induced sepsis; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT Brain, disease
(treating or preventing reperfusion injury of the brain; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT Heart, disease
(treating or preventing reperfusion injury of the myocardium; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT Alzheimer's disease
Atherosclerosis
Cachexia
Cough
Inflammation
Memory disorders
Neoplasm
Osteoarthritis
Osteoporosis
Pain
Parkinson's disease
Psoriasis
Rheumatoid arthritis
Transplant rejection
Urticaria
(treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT Asthma
(treating; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT Inflammation
Intestine, disease
(ulcerative colitis, treating or preventing; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT Mental and behavioral disorders
(unipolar depression, treating or preventing monopolar depression; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)
IT 329900-75-6, COX-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(COX-2 selective inhibitor as co-drugs; preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors for use in combination with other therapeutic agents)

IT **9036-21-9, Phosphodiesterase-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT 791630-50-7P 791630-87-0P 791630-97-2P 791630-98-3P 791631-32-8P
791631-55-5P 791631-61-3P 791631-71-5P 791631-79-3P 791632-08-1P
791632-14-9P 791632-17-2P
RL: **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT 791630-49-4P 791630-51-8P 791630-52-9P 791630-53-0P 791630-54-1P
791630-55-2P 791630-56-3P 791630-57-4P 791630-58-5P 791630-59-6P
791630-60-9P 791630-61-0P 791630-62-1P 791630-63-2P 791630-64-3P
791630-65-4P 791630-66-5P 791630-67-6P 791630-68-7P 791630-69-8P
791630-70-1P 791630-71-2P 791630-72-3P 791630-73-4P 791630-74-5P
791630-75-6P 791630-76-7P 791630-77-8P 791630-78-9P 791630-79-0P
791630-80-3P 791630-81-4P 791630-82-5P 791630-84-7P 791630-85-8P
791630-86-9P 791630-88-1P 791630-89-2P 791630-90-5P 791630-91-6P
791630-92-7P 791630-93-8P 791630-94-9P 791630-95-0P 791630-96-1P
791630-99-4P 791631-00-0P 791631-01-1P 791631-02-2P 791631-03-3P
791631-04-4P 791631-05-5P 791631-06-6P 791631-07-7P 791631-08-8P
791631-09-9P 791631-11-3P 791631-13-5P 791631-15-7P 791631-16-8P
791631-17-9P 791631-18-0P 791631-19-1P 791631-20-4P 791631-21-5P
791631-22-6P 791631-23-7P 791631-24-8P 791631-25-9P 791631-26-0P
791631-27-1P 791631-28-2P 791631-29-3P 791631-30-6P 791631-31-7P
791631-33-9P 791631-34-0P 791631-35-1P 791631-36-2P 791631-37-3P
791631-38-4P 791631-39-5P 791631-40-8P 791631-41-9P 791631-42-0P
791631-43-1P 791631-44-2P 791631-45-3P 791631-46-4P 791631-47-5P
791631-48-6P 791631-49-7P 791631-50-0P 791631-51-1P 791631-52-2P
791631-53-3P 791631-54-4P 791631-56-6P 791631-57-7P 791631-58-8P
791631-59-9P 791631-60-2P 791631-62-4P 791631-63-5P 791631-64-6P
791631-65-7P 791631-66-8P 791631-67-9P 791631-68-0P 791631-69-1P
791631-70-4P 791631-72-6P 791631-73-7P 791631-74-8P 791631-75-9P
791631-76-0P 791631-77-1P 791631-78-2P 791631-80-6P 791631-81-7P
791631-82-8P 791631-83-9P 791631-84-0P 791631-85-1P 791631-86-2P
791631-87-3P 791631-88-4P 791631-89-5P 791631-90-8P 791631-91-9P
791631-92-0P 791631-93-1P 791631-94-2P 791631-95-3P 791631-96-4P
791631-97-5P 791631-98-6P 791631-99-7P 791632-00-3P 791632-01-4P
791632-02-5P 791632-03-6P 791632-04-7P 791632-05-8P 791632-06-9P
791632-07-0P 791632-09-2P 791632-10-5P 791632-11-6P 791632-12-7P
791632-13-8P 791632-15-0P 791632-16-1P 791632-18-3P 791632-19-4P
791632-20-7P 791632-22-9P 791632-26-3P 791632-27-4P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT 56-81-5, Glycerol, reactions 96-50-4, 2-Aminothiazole 104-88-1, 4-Chlorobenzaldehyde, reactions 459-46-1, 4-Fluorobenzyl bromide 459-57-4, 4-Fluorobenzaldehyde 500-22-1, 3-Pyridinecarboxaldehyde 504-29-0, 2-Aminopyridine 583-53-9, 1,2-Dibromobenzene 626-61-9, 4-Chloropyridine 667-27-6, Ethyl bromodifluoroacetate 722-92-9 765-30-0, Cyclopropylamine 872-31-1, 3-Bromothiophene 873-77-8, 4-Chlorophenylmagnesium bromide 922-67-8, Methyl propiolate 2548-79-0, 3-Chlorobenzenecarbothioamide 3446-89-7, 4-Methylthiobenzaldehyde 4858-85-9, 2,3-Dichloropyrazine 6311-37-1, 4-Amino-3-bromobenzoic acid 14047-29-1, 4-Carboxybenzeneboronic acid 16982-21-1, Ethyl thiooxamate 22059-22-9, Acetamidoxime 22179-78-8, 4-Fluoro-N'-

hydroxybenzenecarboximidamide 74003-55-7, 3,4-Dibromobenzaldehyde 89598-96-9, 3-Bromophenylboronic acid 98546-51-1, 4-Methylthiobenzeneboronic acid 149104-90-5, 4-Acetylbenzeneboronic acid 346630-01-1 346630-03-3 791632-21-8, 8-Bromoquinoline-6-carboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

IT 206115-40-4P, 4-Chloro-3-(tributylstannyl)pyridine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 8-(3-biaryl)phenylquinoline **phosphodiesterase-4** inhibitors)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 11 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:878501 HCAPLUS Full-text
DOCUMENT NUMBER: 141:343495
TITLE: The use of phosphodiesterase PDE4D in the screening for medicaments against **atherosclerosis**
INVENTOR(S): Evers, Stefan; Fingerle, Juergen; Himber, Jacques
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004090157	A1	20041021	WO 2004-EP3739	20040407 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004227089	A1	20041021	AU 2004-227089	20040407 <--
CA 2521303	A1	20041021	CA 2004-2521303	20040407 <--
EP 1616024	A1	20060118	EP 2004-726162	20040407 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1771329	A	20060510	CN 2004-80009627	20040407 <--
JP 2006522594	T	20061005	JP 2006-505054	20040407 <--
PRIORITY APPLN. INFO.:			EP 2003-7993 A	20030410 <--
			WO 2004-EP3739 W	20040407

ED Entered STN: 22 Oct 2004
AB The present invention provides the use of PDE4, preferably PDE4D, more preferably PDE4D5 or PDE4D7, as a novel target for the identification of compds. that can be used for the treatment of atherosclerosis, preferably of peripheral arterial occlusive disease (PAOD), or for the treatment of restenosis.
IC ICM C12Q001-34

ICS C07K016-40; C12N009-16; A61K031-00; A61K038-00; A61K039-00; A61P009-00
CC **1-8** (Pharmacology)
Section cross-reference(s): 3, 7, 13
ST phosphodiesterase PDE4D screening human **atherosclerosis** **restenosis** peripheral arterial occlusion
IT Antiarteriosclerotics
(antiatherosclerotics; use of phosphodiesterase PDE4D in screening for medicaments against **atherosclerosis**)
IT **Artery, disease**
(peripheral, occlusion, **treatment** of; use of phosphodiesterase PDE4D in screening for medicaments against **atherosclerosis**)
IT **Artery, disease**
(**restenosis, treatment** of; use of phosphodiesterase PDE4D in screening for medicaments against **atherosclerosis**)
IT **Atherosclerosis**
(**treatment** of; use of phosphodiesterase PDE4D in screening for medicaments against **atherosclerosis**)
IT **Drug screening**
Human
(use of phosphodiesterase PDE4D in screening for medicaments against **atherosclerosis**)
IT **9036-21-9P, Phosphodiesterase 4**
RL: BPN (Biosynthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(PDE4D5, PDE4D7; use of phosphodiesterase PDE4D in screening for medicaments against **atherosclerosis**)
IT **773904-83-9 773904-84-0 773904-85-1 773904-86-2 773904-87-3 773904-88-4 773904-89-5**
RL: PRP (Properties)
(unclaimed protein sequence; use of phosphodiesterase PDE4D in the screening for medicaments against **atherosclerosis**)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 12 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:824055 HCAPLUS Full-text
DOCUMENT NUMBER: 141:330185
TITLE: Gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders
INVENTOR(S): Gonda, Thomas John; Kremmidiotis, Gabriel
PATENT ASSIGNEE(S): Bionomics Limited, Australia
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085675	A1	20041007	WO 2004-AU383	20040326 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1608778	A1	20051228	EP 2004-723453	20040326 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
JP 2006524492	T	20061102	JP 2006-503979	20040326 <--
US 2006246452	A1	20061102	US 2006-550533	20060428 <--
PRIORITY APPLN. INFO.:			AU 2003-901511 A	20030328 <--
			WO 2004-AU383 W	20040326

ED Entered STN: 08 Oct 2004

AB The present invention provides methods of gene expression profiling for diagnosis and treatment of angiogenesis-related disorders. Diseases of the invention include cancer, rhematoid arthritis, diabetic retinopathy, psoriasis, cardiovascular diseases such as atherosclerosis, ischmeic limb disease and coronary heart disease.

IC ICM C12Q001-68

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): **1**, 3

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
((actin related protein 3), homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Molecular chaperones
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(-containing TCP1, subunit 2β, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Synaptobrevins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-like 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Calcitonin receptors
Interleukin 1 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-like protein, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Caldesmon
Presenilins
Thrombospondins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(1, secretory granule, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Connexins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(43, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Kinesins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)

(5B, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT ADP ribosylation factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(8, -like, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(8, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ADAMTS4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ADAMTS9, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(AF5Q31, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ANKH, homolog, mouse, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(API5, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT ADP ribosylation factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ARF-5, sequence homolog; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT ADP ribosylation factor
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ARF-6, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ARPC3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ATRX, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(B cell receptor associated protein 31, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(B-cell CLL lymphoma 10, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT High-mobility group proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(B1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(BAZ1A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BET1, homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Bone morphogenetic protein receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(BMPR2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(BRE, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Complement receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(C1QR1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Phosphoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(C8FW, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CAP (adenylate cyclase-associated protein), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CAPZA1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CBFβ (core-binding factor β subunit), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT CD antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CD106, gene for; gene expression profiling for diagnosis and

treatment of angiogenesis-related disorders)

IT CD antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CD54, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT CD antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CD9, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CDC42EP3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CDK2 associated protein 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CGI-67, sequence homolog; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CHC1L, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CMT2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(COPA, α subunit, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(COPG, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CPR8, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CXC, 4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(CYF1P1, gene for; gene expression profiling for diagnosis and

treatment of angiogenesis-related disorders)

IT Chloride channel
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ClC-4, intracellular, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(DAAM1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(DDEFL1 (development and differentiation enhancing factor-like 1), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(DDX10, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(DDX5, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DIS3, homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(DNA helicase, chromodomain helicase DNA binding protein 4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(DNCI2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(DOCK4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(E-FABP (epidermal fatty acid-binding protein), psoriasis-associated, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(E2F, 3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP

(Properties); BIOL (Biological study); USES (Uses)
(EAP140 (140 kDa estrogen receptor associated protein), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(EHD3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Translation elongation factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ELL-related, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ERAP140 (estrogen receptor associated protein 140); gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ERBB2IP (interacting protein), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ERM (ETS-related mol.), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ERdj5, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ETL, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(F box protein 30; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(FBXL3A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(FKSG14, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(GABPA (GA-binding protein α subunit) 60kDa, gene for; gene expression profiling for diagnosis and **treatment** of

angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(GATA-6, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(GG2-1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(GSA7, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GrpE-like 2, mitochondrial, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Histones
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(H3, family 3A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HDCL, homolog, Drosophila, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HELO1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HES-1 (hairy and enhancer of split 1), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HEY1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HIPB (huntingtin interacting protein B), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HIVEP2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribonucleoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HNRPC, gene for; gene expression profiling for diagnosis and

treatment of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HNRPDL, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HRB2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Heat-shock proteins
Heat-shock proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HSP 40, homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Heat-shock proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(HSPCA, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ICAM-1 (intercellular adhesion mol. 1), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(IFI16 (interferon γ incucible protein 16), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Annexins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(II, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(KLHL4, homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(KLHL5, Drosophila, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(KLHL6, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribosomal proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(L23, a, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribosomal proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)

(L27, A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribosomal proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(L3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribosomal proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(L36, a-like, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LAMP-2 (lysosome-associated membrane protein 2), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(LCHN, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LIMS1, -like domains, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MAD2 (mitotic arrest deficient 2), -like 1, yeast, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MADH7, homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(MAX, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(MCC, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(MCP (membrane cofactor protein), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(MIB, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MIS12, yeast homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Phosphoproteins

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(MK167 (FHA domain) interacting nucleolar, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribosomal proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(MRPS10 (mitochondrial ribosomal protein S10), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Myc1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NAB1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Flavoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NADH dehydrogenase, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NET6, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NFAT2 (nuclear factor of activated T-cell, 2), C1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NOL5A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NSAP1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NUDT4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NUMB, homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NXF1 (nuclear RNA export factor 1), gene for; gene expression

profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Nbak2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Protein motifs
(PH (pleckstrin homol.) domain, family A, member 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(PLU-1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(POH1-like, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(POSH, mouse ortholog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(PRDM2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(PRE13, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Splicing factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(PSF (PTB-associated splicing factor), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PUM1, Drosophila homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Plastins 3, T isoform, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Protein Tyrosine phosphatase type E, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RAB21, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transforming proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RAB6A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transforming proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RAB6C, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Genetic methods
(RACE; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RAD21, S. pombe homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RAI14 (retinoic acid-induced 14), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transforming proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RAN, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RANBP2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RANBP7, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RANBP9, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transforming proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RAP1B, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RBX1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RDC1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP

(Properties); BIOL (Biological study); USES (Uses)
(RE-1 silencing, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RIN2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RNA helicase DDX3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RNA-binding, 3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RNA-binding, TIA-1 cytotoxic granule associated, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RNA-binding, motif protein 9, mouse ortholog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ROD1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribosomal proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(RPLPO, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT PCR (polymerase chain reaction)
(RT-PCR (reverse transcription-PCR); gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Rho GTPase activating protein 5, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribosomal proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(S19, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribosomal proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(S3A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antigens

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SART2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SATB1 (special-AT-rich binding protein 1), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transport proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SCP19A2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SET, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SFRS2IP, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SH3BGRL2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SKP1A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SMARCA2 (SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A member 2), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SMARCA5, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SOX4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(SPRED1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(STAF42, gene for; gene expression profiling for diagnosis and

treatment of angiogenesis-related disorders)

IT Antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(STAG1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(STAT3 (signal transducer and activator of transcription 3), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Sec5, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Sperm specific 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Stress associated endoplasmic reticulum 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Syntenin, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Cyclins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(T, 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TACC1 (transforming acidic coiled-coil 1), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TAFIIs, TAF9, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TBC1D4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TCF-4 (T-cell factor 4), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TCF12, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TERF21P, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TGFB inducible early growth response, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TNFSF10, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transport proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TOMM20, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transforming proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TPT1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TSC22 (TGFβ-stimulated protein 22) , gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TUCAN, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Splicing factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(U4/U6-associated, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribonucleoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(U5 snRNP (U5 snRNA-containing small nuclear ribonucleoprotein), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(Ubiquilin 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(V-1, rat, ortholog, gene for; gene expression profiling for diagnosis

and **treatment** of angiogenesis-related disorders)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(VCAM-1 (vascular cell adhesion mol. 1), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(VCIP135, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(WAC, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(WT1 (Wilms' tumor suppressor 1), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(WW45, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Synaptotagmin
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(XI, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(XIST, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(YWHAZ, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(YWHAZ, tyrosine tryptophan activation protein zeta polypeptide, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Repeat motifs (protein)
(ankyrin repeat, and SOCS box containing 3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Protein motifs
(baculoviral IAP repeat (BIR3), gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Phosphoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(cAMP, ARPP-19, gene for; gene expression profiling for diagnosis and

treatment of angiogenesis-related disorders)

IT Catenins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(cadherin-associated protein, β1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Diagnosis
(cancer; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(capillary morphogenesis 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(cdc23, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antibodies and Immunoglobulins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(chimeric, in modulating angiogenesis; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Scavenger receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(class B, member 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Scavenger receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(class F, member 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Molecular chaperones
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(containing TCP1, subunit 5ε, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT **Artery, disease**
(coronary; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(cullin 4B, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(cysteine and glycine-rich 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ribozymes
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(deoxy, in modulating angiogenesis; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Eye, disease
(diabetic retinopathy; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Translation initiation factors

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(eIF-4G, 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Translation initiation factors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(eIF3, subunit 2β, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(elongation 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(endothelial cell specific mol. 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antibodies and Immunoglobulins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(fragments, in modulating angiogenesis; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(gene MIB; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(gene XIST; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Angiogenesis
Animals
Arteriosclerosis
Canis familiaris
Capra
Cardiovascular system, disease
Cavia porcellus
DNA microarray technology
DNA sequence analysis
DNA sequences
Drug screening
Electrophoresis
Felis catus
Gene expression profiles, animal
Hamster
Human
Human
Molecular cloning
Monkey
Mus
Neoplasm
Nonhuman primate
Oryctolagus cuniculus
Ovis aries
PCR (polymerase chain reaction)
Pan (genus)

Protein sequences
Psoriasis
Rattus
Reverse transcription
Rheumatoid arthritis
Susceptibility (genetic)
cDNA sequences
(gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT mRNA
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT EST (expressed sequence tag)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Aromatic hydrocarbon receptors
Ephrin-B2
Interleukin 8
Leukemia **inhibitory** factor
Radixin
Thrombin receptors
Thrombomodulin
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(glutaredoxins, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(hepatoma derived growth factor related protein 3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antibodies and Immunoglobulins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(humanized, in modulating angiogenesis; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antibodies and Immunoglobulins
Ribozymes
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(in modulating angiogenesis; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Post-transcriptional processing
(interference; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP

(Properties); BIOL (Biological study); USES (Uses)
(karyopherin α, 3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(karyopherin, Importin β1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Protein motifs
(leucine zipper, W2 domain 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Ischemia
(limb disease; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(membrane, EMP1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(membrane, SMAP-5, golgi, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(membrane, SMAP1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(membrane, VMP1, ortholog, mouse, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(membrane, secretory carrier 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Diagnosis
(mol.; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antibodies and Immunoglobulins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(monoclonal, in modulating angiogenesis; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(muscle-bind-like, Drosophila, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(netrin, 4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(neugrin, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(nuclear factor 1B, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nuclear factor erythroid-derived 2, like-, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleoporin, NUP153, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(of inner mitochondrial membrane 17, homolog A, yeast, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, animal
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(oncogene, RAB11A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, animal
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(oncogene, RAB5A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, animal
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(oncogene, RAP2B, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, animal
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(oncogene, jun B, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oncogene, v-kit, Hardy Zuckerman 4 feline sarcoma viral homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oncogene, v-ral, simian leukemia viral, homolog A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oncogene, v-yes-1, Yamaguchi sarcoma viral oncogene homolog 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Cytokine receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(oncostatin M, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(p125, SEC 23 interacting, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT CD59 (antigen)
CD59 (antigen)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(p18-20, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(p66, α, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pellino 1, homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pellota homolog, Drosophila, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(podocalyxin, -like protein, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(potassium channel modulatory factor, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(praja 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Heat-shock proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(protein 5, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(protein disulfide isomerase related protein, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(protein tyrosine phosphatase receptor type K, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Cadherins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(protocadherin, 17, gene for; gene expression profiling for diagnosis

and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prp4, homolog B, yeast, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Translation initiation factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(putative, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(rho GDP dissociation **inhibitor** β, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(scaffolding, TUBA, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Antibodies and Immunoglobulins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(single chain, in modulating angiogenesis; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transport proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(sodium-bicarbonate cotransporter, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transport proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(solute carrier family 38, member 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transport proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(solute carrier family 7 member 11, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transport proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(solute carrier protein family 7, member 2 gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Nexins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(sorting, 9, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(stathmin, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Nuclear receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(subfamily 4 group A member 3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Nucleic acid hybridization
(subtractive, suppression; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(translin associated factor 6, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(translin, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(transmembrane, 4 superfamily member 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, animal
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(tumor suppressor, PDCD4; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Activin receptors
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(type I, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ubiquitin-conjugating, UBCH5A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(ubiquitin-conjugating, UBE2E1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ubiquitin-conjugating, yeast homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(v-Fos, FBJ murine osteosarcoma viral oncogene homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Gene, animal
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(vav; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(yippee, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Protein motifs
(zinc finger, homeobox 1b, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(zinc finger-containing, 317, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(zinc finger-containing, BCL6B, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(zinc finger-containing, ZNF198, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Transport proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(zinc, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(zizimin 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(α-, PROS1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Laminins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(α4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Integrins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(α2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Integrins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(β1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Microglobulins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(β2-, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT Actins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP

(Properties); BIOL (Biological study); USES (Uses)
(γ1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(γ11, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(γ2 subunit; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(γ2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9033-25-4, Methyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-like 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9025-54-1, Adenosylhomocysteine hydrolase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-like, 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9000-95-7, Ectonucleoside triphosphate diphosphohydrolase 9001-64-3, Malate dehydrogenase 9023-06-7, UDP acetylglucosamine pyrophosphorylase 9031-91-8, Glucosamine phosphate acetyltransferase 9074-14-0, Thioredoxin reductase 142805-58-1, Mitogen activated protein kinase kinase 269077-98-7, Chondroitin synthase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9001-85-8, Lysophospholipase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(1-like, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9075-15-4, E.C. 2.4.1.41
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(10, 4, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 37270-64-7, Acyl CoA thioesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2, homolog, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 140879-24-9, Proteasome
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(26S subunit, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9025-77-8, Phosphatidic acid phosphatase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(2B, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT **9036-21-9**, Phosphodiesterase 3

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(3A, cGMP-**inhibited**, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 109136-49-4, Ubiquitin specific protease
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(7, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9028-86-8, ALDEHYDE DEHYDROGENASE
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(9 family, member A1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 258336-77-5, UNC51.2 serine/threonine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(C. elegans, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 37205-63-3, ATP synthase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(FO subunit 6, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 340830-03-7, Receptor tyrosine kinase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(III, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9029-14-5, Methylene tetrahydrofolate dehydrogenase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(NAD+ dependent, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 142805-56-9, Topoisomerase II
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(TOP2A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 191878-64-5 222963-59-9 222963-75-9 222963-80-6 244205-38-7 253423-83-5 253655-59-3 253655-98-0 272762-39-7 295808-29-6 295808-55-8 295808-60-5 324109-15-1 358405-84-2 441110-17-4 479802-10-3 479802-38-5 479838-40-9, Phospholipase A2 (human isoenzyme γ) 479916-46-6 479926-75-5 479934-71-9 480067-78-5, Protein (human clone IMAGE:4052238) 480078-87-3 480084-87-5 480694-74-4 481141-08-6 481217-41-8 518114-36-8, Protein (human gene MIB) 582939-17-1 606793-69-5
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 96282-35-8, Serine proteinase **inhibitor**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(clade E, member 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9025-42-7, Mannosidase α
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(class 2A member 1, 1A, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9027-03-6, Ubiquinol cytochrome c reductase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(core protein 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9033-53-8, Retinol dehydrogenase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(cytosolic, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9068-38-6, Reverse transcriptase
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 77537-85-0, α2,3-Sialyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9000-83-3, ATPase 9028-35-7, 3-Hydroxy-3-methylglutaryl Coenzyme A reductase 9032-20-6, Quinone reductase 9032-88-6, Fumarate hydratase 9035-58-9, Blood coagulation factor III 9039-45-6, Deoxycytidine kinase 9047-22-7, Cathepsin B 9059-37-4, Nucleoside phosphorylase 37237-44-8, UDP glucose ceramide glucosyltransferase 37278-21-0, UMP CMP kinase 50936-59-9, Iduronate 2 sulfatase 53570-84-6, Cytochrome b561 60321-03-1, Tubulin tyrosine ligase 64885-84-3, Spermidine acetyltransferase 108022-16-8, Endo-α-mannosidase 123626-67-5, Endothelin 1 133249-52-2, Thymine-DNA glycosylase 137632-08-7, Mitogen-activated protein kinase 1 146702-84-3, Mitogen activated protein kinase kinase kinase 1 151821-62-4, Ubiquitin C 152478-56-3, Janus kinase 1 178037-70-2, Protein kinase sgk-1 194368-66-6, Angiopoietin 2 213903-53-8, Cryptochrome 1 306298-47-5, Dual specificity protein phosphatase 1 324752-01-4, Stanniocalcin 1 329967-85-3 644990-62-5, Peroxiredoxin 3 681457-74-9, Cytochrome P450 1
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 148463-92-7, Metalloprotease STE24
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(homolog, yeast, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9001-84-7, Phospholipase A2
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(intracellular membrane-associated calcium independent, γ isoenzyme, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 76901-00-3, Platelet activating factor acetylhydrolase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(isoform 1b, β subunit, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 50812-37-8, Glutathione S transferase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(microsomal, isoenzyme 2, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 140081-63-6 171845-09-3 220500-43-6 225718-47-8 247560-30-1
247561-18-8 251518-18-0, DNA (human clone DKFZp434G0972 cDNA)
259479-07-7 259514-03-9 266667-20-3 266667-46-3 266667-51-0
270550-49-7 280540-69-4 288836-72-6 292544-95-7 292561-29-6
321122-76-3 356828-39-2 358026-38-7 360810-42-0 363546-60-5
366429-20-1, DNA (human clone PEBLM1000174 cDNA) 381984-71-0
381986-94-3 390116-80-0, DNA (human clone DKFZp564F053 cDNA)
390331-59-6, DNA (human clone PLACE4000445 cDNA) 392070-71-2
392070-73-4 392093-07-1 392105-51-0 392112-53-7 392198-82-2
398299-70-2 398302-11-9 398399-21-8 398399-85-4 423870-73-9
439771-95-6 439778-33-3 439779-47-2 441608-06-6, DNA (human clone
MESAN2006401 cDNA) 441640-02-4, DNA (human clone CTONG2000469 cDNA)
441642-11-1, DNA (human clone D9OST2000440 cDNA) 450507-65-0
450510-97-1 496346-79-3, DNA (human gene MIB cDNA) 537432-01-2
577668-43-0 582939-16-0 606793-68-4 767014-14-2 767014-15-3
767014-16-4 767014-17-5 767014-18-6 767014-19-7 767014-20-0
767014-27-7 767014-28-8 767014-29-9 767014-30-2 767014-31-3
767014-32-4 767014-33-5 767014-34-6 767014-35-7 767014-36-8
767014-37-9 767014-38-0 767014-39-1 767014-40-4 767014-41-5
767014-42-6 767014-43-7 767014-44-8 767014-45-9 767014-46-0
767014-47-1 767014-48-2 767014-49-3 767014-50-6 767014-51-7
767014-52-8 767014-53-9 767014-54-0 767014-55-1 767014-56-2
767014-57-3 767014-58-4 767014-59-5 767014-60-8 767014-61-9
767014-62-0 767014-63-1
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9079-67-8, NADH dehydrogenase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(subuit 4L, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 9001-16-5, Cytochrome C oxidase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(subunit II, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 79747-53-8, Protein tyrosine phosphatase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(type IVA, member 1, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 142008-29-5, CAMP-dependent protein kinase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(type Iα, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 767016-50-2 767016-51-3 767016-52-4 767016-53-5 767016-54-6
767016-55-7
RL: PRP (Properties)
(unclaimed nucleotide sequence; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 767016-56-8 767016-57-9 767016-58-0 767016-59-1 767016-60-4
767016-62-6 767016-63-7 767016-64-8
RL: PRP (Properties)
(unclaimed protein sequence; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 366806-33-9, Casein kinase 2
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP

(Properties); BIOL (Biological study); USES (Uses)
(α' polypeptide, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

IT 105238-46-8, Macropain
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(β type 1, subunit β type 3, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

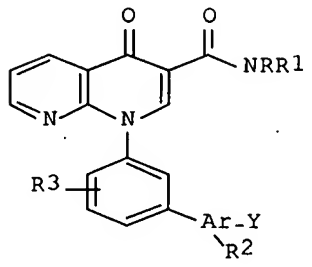
IT 57285-09-3, Inhibin
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(βA, gene for; gene expression profiling for diagnosis and **treatment** of angiogenesis-related disorders)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

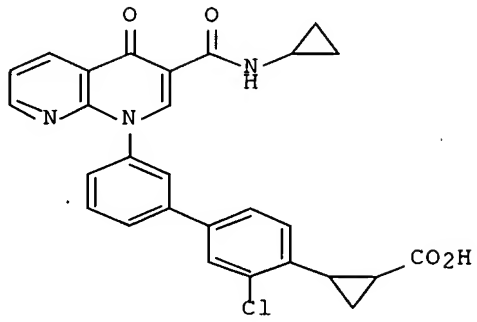
L76 ANSWER 13 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:467889 HCAPLUS Full-text
DOCUMENT NUMBER: 141:38596
TITLE: Preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors
INVENTOR(S): Dube, Daniel; Gallant, Michel; Lacombe, Patrick; Aspiotis, Renee; Dube, Laurence; Girard, Yves; MacDonald, Dwight
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004048374	A1	20040610	WO 2003-CA1800		20031119 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2506648	A1	20040610	CA 2003-2506648		20031119 <--
AU 2003283167	A1	20040618	AU 2003-283167		20031119 <--
EP 1565464	A1	20050824	EP 2003-775029		20031119 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003016458	A	20051011	BR 2003-16458		20031119 <--
CN 1738819	A	20060222	CN 2003-80108952		20031119 <--
JP 2006508989	T	20060316	JP 2004-554102		20031119 <--
US 2005107402	A1	20050519	US 2004-764229		20040123 <--
US 2006058316	A1	20060316	US 2005-534582		20050511 <--
NO 2005003046	A	20050727	NO 2005-3046		20050621 <--
PRIORITY APPLN. INFO.:			US 2002-428611P	P	20021122 <--
			WO 2003-CA1800	W	20031119 <--

OTHER SOURCE(S): MARPAT 141:38596
ED Entered STN: 10 Jun 2004
GI



I



II

AB Title compds. [I; Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl; Y = CO2R4, ACO2R4, etc.; A = alkyl; R, R4 = H, alkyl; R1 = H, (substituted) alkyl, cycloalkyl, alkoxy, alkenyl, alkynyl, heteroaryl, heterocyclyl; R2 = H, halo, cyano, NO2, (substituted) alkyl, cycloalkyl, alkoxy, Ph, heteroaryl, amino, etc.; R3 = H, halo, cyano, NO2, (substituted) alkyl, cycloalkyl, etc.], were prepared Thus, title compound (II) (preparation outlined) inhibited PDE4-mediated hydrolysis of cAMP to AMP with IC50 = 0.1 nM.

IC ICM C07D471-04
ICS A61K031-4375; A61P025-00; C07D221-00

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT Inflammation
(Crohn's disease, treatment; preparation of biphenylnaphthyridonecarboxamide s as **phosphodiesterase-4** inhibitors)

IT Intestine, disease
(Crohn's, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Antihistamines
(H1, coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Muscarinic antagonists
(M2, coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Muscarinic antagonists
(M3, coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Respiratory distress syndrome
(adult, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Allergy
Inflammation

Nose, disease
(allergic rhinitis, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Inflammation
Spinal column, disease
(ankylosing spondylitis, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Dermatitis
(atopic, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Sepsis
(bacterial, viral, fungal treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Leukotrienes
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biosynthesis inhibitors, coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Bronchi, disease
Inflammation
(chronic bronchitis, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Inflammation
Kidney, disease
(chronic glomerulonephritis, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Lung, disease
(chronic obstructive pulmonary disease, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Leukotriene antagonists
β2-Adrenoceptor agonists
(coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Corticosteroids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Abdomen, disease
(colic, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Animal tissue
(cytokine mediated degeneration, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Nervous system, disease
(degeneration, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Mental and behavioral disorders
(depression, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Granuloma

(eosinophilic, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Gastric acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gastric acid hypersecretion treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Neoplasm
(growth, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Injury
(head and neck, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Arthritis
(inflammatory arthritis treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Head and Neck, disease
Reperfusion
(injury, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Hoof, disease
Inflammation
(laminitis, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Memory disorders
(memory retention defect, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Neoplasm
(metastasis, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Inflammation
(neurogenic, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Respiratory distress syndrome
(newborn, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Anti-inflammatory agents
(nonsteroidal, coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidepressants
Antiparkinsonian agents
Antitussives
Cognition enhancers
Human
(preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT Injury
(reperfusion, treatment; preparation of biphenylnaphthyridonecarboxamides

as
phosphodiesterase-4 inhibitors)
IT **Artery, disease**
(**restenosis**, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)
IT Shock (circulatory collapse)
(septic, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)
IT Spinal cord, disease
(trauma, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)
IT Osteoporosis
(treatment of; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)
IT Alzheimer's disease
Asthma
Atherosclerosis
Cachexia
Cough
Diabetes insipidus
Inflammation
Multiple sclerosis
Neoplasm
Osteoarthritis
Pain
Parkinson's disease
Psoriasis
Rheumatoid arthritis
Skin, disease
Transplant rejection
Urticaria
(treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)
IT Inflammation
Intestine, disease
(ulcerative colitis, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)
IT Muscle, disease
(wasting, treatment; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)
IT 329900-75-6, COX-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(COX-2 inhibitors coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)
IT 702639-52-9P 702639-53-0P 702639-54-1P 702639-55-2P 702639-56-3P
702639-57-4P 702639-58-5P 702639-59-6P 702639-60-9P 702639-61-0P
702639-62-1P 702639-63-2P 702639-64-3P 702639-65-4P 702639-66-5P
702639-67-6P 702639-69-8P 702639-71-2P 702639-73-4P 702639-74-5P
702639-76-7P 702639-78-9P 702639-80-3P 702639-81-4P 702639-83-6P
702639-85-8P 702639-86-9P 702639-88-1P 702639-90-5P 702639-91-6P
702639-93-8P 702639-95-0P 702639-96-1P 702639-98-3P 702640-00-4P
702640-02-6P 702640-04-8P 702640-06-0P 702640-08-2P 702640-10-6P
702640-12-8P 702640-13-9P 702640-15-1P 702640-16-2P 702640-17-3P
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702640-28-6P 702640-29-7P 702640-30-0P 702640-31-1P 702640-32-2P
702640-33-3P 702640-34-4P 702640-35-5P 702640-36-6P 702640-37-7P

702640-38-8P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT 9028-35-7
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitors, statins, coadministration; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT **9036-21-9, Phosphodiesterase-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT 702640-46-8P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT 753-90-2, 2,2,2-Trifluoroethylamine 1927-95-3 2516-47-4, Cyclopropylmethylamine 3132-99-8, 3-Bromobenzaldehyde 4701-17-1, 5-Bromothiophene-2-carboxaldehyde 6940-50-7, 4-Bromomandelic acid 26394-96-7 31938-07-5 34919-34-1 57848-46-1, 4-Bromo-2-fluorobenzaldehyde 78775-11-8, 4-Bromo-3-methylbenzaldehyde 81606-47-5 158435-41-7, 4-Bromo-2-chlorobenzaldehyde 196311-65-6, 1-Aminocyclopropanecarbonitrile 220731-02-2, Ethyl 2-chloronicotinoylacetate 345965-52-8 477251-96-0 638220-48-1 701263-25-4 702640-50-4 702640-57-1 702640-59-3 702640-62-8 702640-64-0 702640-66-2 702640-68-4 702640-70-8 702640-72-0 702640-73-1 702640-74-2 702640-76-4 702640-77-5 702640-79-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

IT 477251-77-7P 477251-78-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of biphenylnaphthyridonecarboxamides as **phosphodiesterase-4** inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 14 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:368876 HCAPLUS Full-text
DOCUMENT NUMBER: 140:368737
TITLE: Methods of use of inhibitors of phosphodiesterases and modulators of nitric oxide, reactive oxygen species, and metalloproteinases in the treatment of Peyronie's disease, **arteriosclerosis** and other fibrotic diseases
INVENTOR(S): Gonzalez-Cadavid, Nestor F.; Rajfer, Jacob
PATENT ASSIGNEE(S): Harbor-UCLA Research and Education Institute, USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004037183	A2	20040506	WO 2003-US33400		20031021 <--
WO 2004037183	A3	20040805			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003286555	A1	20040513	AU 2003-286555		20031021 <--
US 2005085486	A1	20050421	US 2004-779069		20040213 <--
PRIORITY APPLN. INFO.:			US 2002-420281P	P	20021022 <--
			WO 2003-US33400	W	20031021 <--

ED Entered STN: 06 May 2004

AB The methods and compns. of the invention are of use for treatment of conditions involving fibrosis, such as Peyronie's disease plaque, penile corporal fibrosis, penile veno-occlusive dysfunction, Dupuytren's disease nodules, vaginal fibrosis, clitoral fibrosis, female sexual arousal disorder, abnormal wound healing, keloid formation, general fibrosis of the kidney, bladder, prostate, skin, liver, lung, heart, intestines or any other localized or generalized fibrotic condition, vascular fibrosis, arterial intima hyperplasia, atherosclerosis, arteriosclerosis, restenosis, cardiac hypertrophy, hypertension or any condition characterized by excessive fibroblast or smooth muscle cell proliferation or deposition of collagen and extracellular matrix in the blood vessels and/or heart. In certain embodiments, the compns. may comprise a PDE-4 inhibitor, PDE-5 inhibitor, a compound that elevates cGMP and/or PKG, a stimulator of guanylyl cyclase and/or PKG, a combination of a compound that elevates cGMP, PKG or NO with an antioxidant that decreases ROS, or a compound that increases MMP activity. In certain embodiments, the composition may be a gene therapy vector.

IC ICM A61K

CC **1-12** (Pharmacology)
Section cross-reference(s): 63

IT cDNA
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(PKG; phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

IT **Artery, disease**
(intima, hyperplasia; phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

IT Antiarteriosclerotics
Antihypertensives
Antioxidants
Apoptosis
Arteriosclerosis
Atherosclerosis
Cardiovascular agents
Cell proliferation
Fibrosis
Gastrointestinal agents
Gene therapy
Genetic vectors

Human
Hypertension
Keloid
Wound healing promoters
(phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

IT Antisense RNA
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

IT **Artery, disease**
(**restenosis**; phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

IT Double stranded RNA
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(small interfering; phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

IT 7665-99-8, Cyclic GMP 7782-44-7D, Oxygen, reactive species 9025-82-5, Phosphodiesterase **9036-21-9**, Phosphodiesterase IV 9054-75-5, Guanyl cyclase 9068-52-4, Phosphodiesterase V 10102-43-9, Nitric oxide, biological studies 77642-24-1, Thymosin .beta.**4** 87397-91-9, Thymosin β10 89964-14-7, Prothymosin α 125978-95-2, Nitric oxide synthase 140208-23-7, PAI-1 141588-27-4, Protein kinase G 141907-41-7, Matrix metalloproteinase 146480-35-5, Matrix metalloproteinase 2 146480-36-6, Matrix metalloproteinase 9 501433-35-8, Inducible nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**phosphodiesterases** inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

IT 31356-94-2, 8-Bromo-cyclic GMP 67776-06-1, SNAP
RL: **PAC (Pharmacological activity)**; BIOL (Biological study)
(phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

IT 6493-05-6, Pentoxifylline 61413-54-5, Rolipram 61512-21-8D, Thymosin, derivs. 139755-83-2, Sildenafil 171596-29-5, Tadalafil 224785-90-4, Vardenafil
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

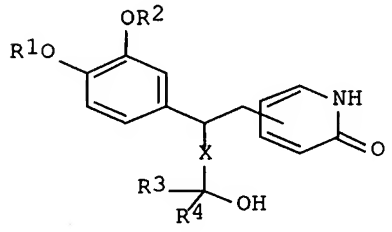
IT 61512-21-8, Thymosin
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(thymosin-family peptides; phosphodiesterases inhibitors and modulators of NO, reactive oxygen species, and metalloproteinases for treatment of fibrotic diseases)

L76 ANSWER 15 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41444 HCAPLUS Full-text
DOCUMENT NUMBER: 140:111282
TITLE: Preparation of diarylethylpyridones as **phosphodiesterase-4** (PDE4) inhibitors
INVENTOR(S): Cote, Bernard; Martins, Evelyn

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005258	A1	20040115	WO 2003-CA995	20030702 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2490097	A1	20040115	CA 2003-2490097	20030702 <--
AU 2003281219	A1	20040123	AU 2003-281219	20030702 <--
EP 1519922	A1	20050406	EP 2003-739922	20030702 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005538972	T	20051222	JP 2004-518321	20030702 <--
US 2006004056	A1	20060105	US 2005-518294	20050801 <--
PRIORITY APPLN. INFO.:			US 2002-393281P P	20020702 <--
			WO 2003-CA995 W	20030702 <--

OTHER SOURCE(S): MARPAT 140:111282
ED Entered STN: 18 Jan 2004
GI



I

AB Title compds. [I; X = Ph, pyridinyl, thiazolyl, pyrimidinyl, pyridazinyl, furyl, thienyl, oxazolyl, isoxazolyl, isothiazolyl; R1, R2 = (halo-substituted) alkyl, cycloalkyl; R3, R4 = (halo-substituted) alkyl, cycloalkyl, aryl, heteroaryl; R3R4 = atoms to form a ring], were prepared I [e.g., 5-[2-[3,4-bis(difluoromethoxy)phenyl]-2-[4-(1,1,1,3,3,3-hexafluoro- 2-hydroxypropan-2-yl)phenyl]ethyl]-2-pyridone, preparation outlined] inhibited PDE4a with IC50 = 0.05-200 nM.

IC ICM C07D213-64
ICS C07D417-06; A61K031-4412; A61K031-4439; A61K031-444; A61P011-06;

A61P029-00
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
ST arylethylpyridone prepn **phosphodiesterase 4** inhibitor; PDE4 inhibitor diarylethylpyridone; asthma bronchitis chronic obstructive pulmonary disease treatment arylethylpyridone prepn; adult respiratory distress syndrome treatment arylethylpyridone prepn; cough ulcerative colitis Crohn disease treatment diarylethylpyridone prepn
IT Corticosteroids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(coadministration; preparation of diarylethylpyridones as PDE4 inhibitors)
IT **Artery, disease**
(**restenosis**, treatment; preparation of diarylethylpyridones as PDE4 inhibitors)
IT Alzheimer's disease
Asthma
Atherosclerosis
Cachexia
Cough
Inflammation
Multiple sclerosis
Neoplasm
Neoplasm
Osteoarthritis
Osteoporosis
Pain
Parkinson's disease
Psoriasis
Rheumatoid arthritis
Sepsis
Transplant rejection
Urticaria
(treatment; preparation of diarylethylpyridones as PDE4 inhibitors)
IT 9028-35-7
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitors, statins, coadministration; preparation of diarylethylpyridones as PDE4 inhibitors)
IT **9036-21-9**, Pde4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of diarylethylpyridones as PDE4 inhibitors)
IT 552287-68-0P 645419-28-9P 645419-29-0P 645419-30-3P 645419-31-4P 645419-32-5P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diarylethylpyridones as PDE4 inhibitors)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 16 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:739986 HCAPLUS Full-text
DOCUMENT NUMBER: 141:265962
TITLE: Pharmaceutical compositions containing deprenyl and proparglamine compounds to prevent toxicity of antiinflammatory agents and enhance their efficacy
INVENTOR(S): Thomas, Thomas Nadackal
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S. Ser. No. 137,342.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004176469	A1	20040909	US 2004-802000	20040316 <--
US 6432991	B1	20020813	US 2000-881199	20000727 <--
US 2002128299	A1	20020912	US 2002-137342	20020503 <--
US 6635667	B2	20031021		
US 2005009835	A1	20050113	US 2004-881911	20040630 <--
PRIORITY APPLN. INFO.:			US 2000-881199 A2	20000727 <--
			US 2002-61734 B2	20020201 <--
			US 2002-137342 A2	20020503 <--
			US 1998-72718P P	19980127 <--
			WO 1999-US1670 A2	19990126 <--
			US 2003-486121P P	20030711 <--
			US 2004-802000 A1	20040316

OTHER SOURCE(S): MARPAT 141:265962
ED Entered STN: 10 Sep 2004
AB Disclosed is pharmacol. effects of deprenyl or propargylamine compds. (monoamine oxidase, MAO inhibitors) and novel compns. comprising at least one MAO inhibitor and at least one antiinflammatory agent such as nonsteroidal antiinflammatory drugs (NSAIDS), steroids, acetaminophen (COX-3 inhibitors), 5-lipoxygenase inhibitors, leukotriene receptor antagonists, leukotriene A4 hydrolase inhibitors, antihistaminics, histamine 2 receptor antagonists, phosphodiesterase-4 antagonists, cytokine antagonists, CD44 antagonists, antineoplastic agents, 3-hydroxy-3-methylglutaryl CoA inhibitors (statins), estrogens, androgens, antiplatelet agents, antidepressants, Helicobacter pylori inhibitors, proton pump inhibitors, thiazolidinediones, dual-action compds., combinations of these drugs with other agents, derivs. and metabolites of synthetic and natural antiinflammatory agents. The compds. and compns. protect against gastrointestinal, renal and other toxicities induced by antiinflammatory agents, and enhance the beneficial effects of these drugs. Effects of MAO inhibitors such as l-deprenyl co-administered with antiinflammatory drugs or chemical attached to antiinflammatory drugs are disclosed. Therapeutic methods of using MAO inhibitors and antiinflammatory drugs for the prevention and treatment of inflammatory disorders, pain, fever, cancer, gastrointestinal lesions, and a variety of cardiac, cerebral and peripheral disorders are disclosed. For example, when 1-deprenyl 100 mg was given 5 min. before the aspirin 200 mg, the analgesic activity was not reduced, but the gastric lesion caused by aspirin was reduced.
IC ICM A61K031-137
INCL 514649000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 4
IT Allergy
Alzheimer's disease
Analgesics
Angiogenesis
Anti-inflammatory agents
Antidepressants
Antihistamines
Antitumor agents
Arthritis
Asthma
Atherosclerosis
Blood vessel, disease
Cardiovascular system, disease

Central nervous system, disease
Combination chemotherapy
Diabetes mellitus
Digestive tract, disease
Leukotriene antagonists
Muscle, disease
Neoplasm
Pet animal
Platelet aggregation inhibitors
Polycythemia vera
Urinary system, disease
α-Adrenoceptor antagonists
β-Adrenoceptor antagonists
(pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

IT Androgens
Estrogens
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

IT Amides, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

IT Steroids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

IT Transport proteins
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(proton pump, inhibitors; pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

IT **9036-21-9, Phosphodiesterase-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

IT 9028-35-7
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitors, statins; pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

IT 2295-31-0D, Thiazolidinedione, derivs. 753003-20-2 753003-21-3 753003-22-4 753003-23-5 753003-24-6
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

IT 51-12-7, Nialamide 51-71-8, Phenelzine 54-92-2, Iproniazid 83-89-6, Quinacrine 103-90-2 155-09-9, Tranyl cypromine 302-01-2, Hydrazine, biological studies 555-57-7, Pargyline 2323-36-6, Deprenyl 2450-71-7D, Propargylamine, derivs., conjugates with NSAIDS 4528-51-2

14611-51-9, Selegiline 17780-72-2, Clorgyline 35161-71-8, N-Methyl propargylamine 94319-79-6, RO 16-6491 103878-84-8, Lazabemide 127500-84-9, RO 41-1049 136236-51-6, Rasagiline 143347-01-7
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing deprenyl and proparglamine compds. in combination with antiinflammatory agents for less toxicity and better efficacy for inflammation-related diseases)

L76 ANSWER 17 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:609928 HCAPLUS Full-text
DOCUMENT NUMBER: 141:134090
TITLE: Compositions and methods for **inhibiting** platelet activation and thrombosis
INVENTOR(S): Flaumenhaft, Robert Charles
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, USA
SOURCE: U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of Appl. No. PCT/US02/19843.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004147540	A1	20040729	US 2003-740182	20031218 <--
US 7166612	B2	20070123		
WO 2003001968	A2	20030109	WO 2002-US19843	20020624 <--
WO 2003001968	A3	20030925		
WO 2003001968	A8	20040408		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2007060605	A1	20070315	US 2006-595130	20061108 <--
PRIORITY APPLN. INFO.:			US 2001-300932P	P 20010626 <--
			WO 2002-US19843	A2 20020624 <--
			US 2003-740182	A1 20031218 <--

OTHER SOURCE(S): MARPAT 141:134090
ED Entered STN: 30 Jul 2004
AB The invention provides methods and compns. for reducing platelet activation, platelet aggregation and thrombosis. The invention further provides compns. and methods for treating or preventing diseases or disorders in which the pathol. of the disease or disorder involves one or more of platelet activation, platelet aggregation and thrombus formation. The invention addnl. relates to the use of protein palmitoylation inhibitors for the reduction of platelet activation, platelet aggregation and thrombosis, as well as to the use of protein palmitoylation as a target for the identification of inhibitors of platelet activation, platelet aggregation and thrombosis.
IC ICM A61K031-473
INCL 514290000
CC **1-8** (Pharmacology)
ST platelet activation **inhibitor** thrombosis **treatment**; protein palmitoylation **inhibitor** platelet activation

inhibition

IT Selectins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P-, expression; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Heart, disease
(angina pectoris; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Heart, disease
(atrial fibrillation, thrombosis in; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Brain, disease
(cerebrovascular; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Anticoagulants
Cell activation
Cell aggregation
Combination chemotherapy
Human
Ischemia
Platelet (blood)
Platelet aggregation **inhibitors**
Thrombosis
(compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT **Drug screening**
Palmitoylation
(compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and **drug screening** using palmitoyl acetyltransferase)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and **drug screening** using palmitoyl acetyltransferase)

IT Heart, disease
(infarction; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Placenta, disease
(insufficiency; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Blood vessel, disease
(peripheral; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Medical goods
(stents, placement, thrombosis in; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Allergy
Atherosclerosis
Coronary angioplasty
Coronary bypass surgery
Inflammation
Surgery
Wound healing
(thrombosis in; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Heart
(valve, artificial, insertion, thrombosis in; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αIIbβ3, **inhibitors**; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT 111789-90-3
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT 50-78-2, Aspirin 26303-23-1 36725-41-4 54258-41-2, 1,10-Phenanthrolin-5-amine 55142-85-3, Ticlopidine 61468-81-3D, aryl derivs. 83568-05-2 107940-86-3 113665-84-2, Clopidogrel 143653-53-6, Abciximab 144494-65-5, Tirofiban 188627-80-7, Eptifibatide 312926-53-7 317335-73-2 481686-99-1 481687-00-7 481687-01-8 487013-41-2 487013-57-0 487014-14-2 487014-24-4 499190-09-9 499190-10-2 499190-12-4 727695-15-0D, alkyl derivs. 727695-16-1
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

IT 1763-10-6, Palmitoyl CoA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and **drug screening** using palmitoyl acetyltransferase)

IT 122544-67-6, Protein palmitoyltransferase
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and **drug screening** using palmitoyl acetyltransferase)

IT **9036-21-9**, CAMP phosphodiesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; compns. and methods for **inhibiting** platelet activation and aggregation and thrombosis in relation to protein palmitoylation **inhibition** and combination with other agents)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 18 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:912990 HCAPLUS Full-text
DOCUMENT NUMBER: 139:375014
TITLE: Methods and compositions with N-phenyl-2-pyrimidine compounds **inhibiting** platelet derived growth factor receptor for the **treatment** of graft failure
INVENTOR(S): Sukhatme, Vikas P.
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003094904	A1	20031120	WO 2003-US314916	20030513 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003232115	A1	20031111	AU 2003-232115	20030513 <--
CA 2490989	A1	20031120	CA 2003-2490989	20030513 <--
EP 1509219	A1	20050302	EP 2003-750120	20030513 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005533019	T	20051104	JP 2004-502990	20030513 <--
US 2005261283	A1	20051124	US 2005-514322	20050719 <--
PRIORITY APPLN. INFO.:			US 2002-380180P P	20020513 <--
			US 2003-464023P P	20030418 <--
			WO 2003-US14916 W	20030513 <--

OTHER SOURCE(S): MARPAT 139:375014
ED Entered STN: 21 Nov 2003
AB The present invention provides methods and compns. for treating graft failure resulting from neointimal hyperplasia. These methods and compns. feature the use of platelet derived growth factor receptor (PDGFR) inhibitor compds., such as N-phenyl-2-pyrimidine compds. (e.g., imatinib mesylate) to inhibit the biol. activity of the PDGFR and treat AV graft failure. Gleevec and rapamycin inhibited smooth muscle cell migration.
IC ICM A61K031-165
ICS A61K031-505; A61K038-21
CC **1-8** (Pharmacology)
Section cross-reference(s): 28, 63
ST graft failure **treatment** phenyl pyrimidine compd; platelet derived growth factor receptor **inhibitor** graft failure; neointimal hyperplasia graft failure **treatment**; imatinib mesylate **inhibition** PDGFR graft failure; Gleevec rapamycin **inhibition** smooth muscle cell migration
IT Thrombospondins

RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(1, angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Cadherins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5, angiogenesis **inhibitor** blocking extracellular domain of, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Platelet-derived growth factors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(BB, **inhibition** of PDGFR activity stimulated by; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD106, immunosuppressant agent **inhibiting**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Drug delivery systems
Drug screening
Human
(N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Platelet-derived growth factor receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Polymers, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Selectins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P-, immunosuppressant agent **inhibiting**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PIH12, angiogenesis **inhibitor** blocking signaling by, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PSGL-1 (P-selectin glycoprotein ligand-1), immunosuppressant agent **inhibiting**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Transforming growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TGF-β receptor, type I, antibody to, as antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Transforming growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TGF-β receptor, type II, antibody to, as antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Transforming growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TGF-β receptor, type III, antibody to, as antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Tyrosine kinase receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Tie-1, angiogenesis **inhibitor** blocking signaling by, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Tyrosine kinase receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Tie-2, angiogenesis **inhibitor** blocking signaling by, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VCAM-1 (vascular cell adhesion mol. 1), immunosuppressant agent **inhibiting**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Drug interactions
(additive, in **inhibition** of smooth muscle cell migration by Gleevec and rapamycin; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(angiogenesis **inhibitor** antibody to, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Proteins
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiangiogenic, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Fibrosis
(antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds.
inhibiting platelet derived growth factor receptor for

treatment of graft failure)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antigens Mac-1 (macrophage 1), immunosuppressant agent **inhibiting**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 5-HT antagonists
(antimigratory compds., composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Artery
(aorta, screening for compds. reducing migration of vascular smooth muscle cells of; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Hyperplasia
(arterial intimal, graft failure due to; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Blood vessel
(arteriovenous anastomosis, for vascular access for hemodialysis; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Blood vessel
(artificial, for access in hemodialysis; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Tea products
(beverages, green, angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Signal transduction, biological
(by TIE-1 or TIE-2, angiogenesis **inhibitor** blocking, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Angiogenesis **inhibitors**
Cytotoxic agents
Immunosuppressants
Platelet aggregation **inhibitors**
(composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Drug delivery systems
(composites, of microsphere embedded in hydrophobic matrix; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Microspheres
(embedded in hydrophobic matrix, N-phenyl-2-pyrimidine derivative dispersed in composite system of; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Endothelin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endothelin 1, antagonists, antimigratory compds., composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Protein motifs
(extracellular domain of VE cadherin, agent blocking, as angiogenesis

inhibitor, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Transplant and Transplantation
(failure, **treatment** of; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Drug delivery systems
(films; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Extracellular matrix
(graft failure characterized by deposition of; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Thrombosis
(graft failure from; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Fluoropolymers, biological studies
RL: TEM (Technical or engineered material use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(graft in vascular access for hemodialysis; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Polyester fibers, biological studies
RL: TEM (Technical or engineered material use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(graft of; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Dialysis
(hemodialysis, graft used for vascular access in; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Macrophage
(immunosuppressant agent interfering with function of, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT CTLA-4 (antigen)
Interleukin 2 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunosuppressant antibody to, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT **Artery, disease**
(intima, hyperplasia, graft failure due to; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Drug delivery systems
(microspheres; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Peptides, biological studies
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(of antiangiogenic proteins, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Cell migration
(of smooth muscle cells into intima in graft failure; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Cell proliferation
(of vascular smooth muscle cells in graft failure; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Arrestins
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(peptide as angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Blood vessel, disease
(peripheral, graft used to **treat**; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Proteins
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(restin (Reed-Steinberg cell-expressed intermediate filament-associated), angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Ribosome-inactivating proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(saporin, conjugates, with bFGF, antiproliferative antibody to, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Muscle
(smooth, graft failure characterized by migration into intima of cells of; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT **Artery, disease**
(stenosis, graft failure from; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Medical goods
(sutures; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Blood vessel
(tunica intima, graft failure characterized by migration of smooth muscle cells into; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Interferons
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(α, angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αIIbβ3, **inhibitors**, antiplatelet agent, composition

further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α4β1, immunosuppressant agent **inhibiting**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-, agent **inhibiting** signaling by, as antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Transforming growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-transforming growth factor, antibody to, as antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT Platelet-derived growth factor receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(β; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 57356-49-7D, compds. 152459-95-5 220127-57-1, Imatinib mesylate
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 189460-40-0, Connective tissue growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agent blocking signaling by, as antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 62571-86-2, Captopril
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(angiogenesis **inhibitor** and antiproliferative agent, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 50-18-0, Cytoxan
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(angiogenesis **inhibitor** and immunosuppressant, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 127464-60-2, Vascular endothelial growth factor
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(angiogenesis **inhibitor** antibody to VEGF receptor blocking binding of, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for

treatment of graft failure)

IT 489395-96-2, VEGF-A
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(angiogenesis **inhibitor** antibody to, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 50-35-1, Thalidomide 52-67-5, Penicillamine 60-54-8, Tetracycline 66-22-8, Uracil, biological studies 362-07-2, 2-Methoxyestradiol 446-72-0, Genistein 458-37-7, Curcumin 501-36-0, Resveratrol 616-91-1, N-Acetylcysteine 865-21-4, Vinblastine 17902-23-7, Tegafur 37270-94-3, Platelet factor 4 70641-51-9, Edelfosine 86090-08-6, Angiostatin 129298-91-5, TNP-470 162011-90-7, VIOXX 169590-42-5, CELEBREX 187888-07-9, Endostatin 216974-75-3, AVASTIN 624745-50-2, CPTK 787 624745-51-3, SFH 1
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 64-86-8, Colchicine 6493-05-6, Pentoxifylline 53179-13-8, Pirfenidone 65666-07-1, Silymarin 170277-31-3, Remicade 185243-69-0, Embrel
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds.
inhibiting platelet derived growth factor receptor for **treatment** of graft failure)

IT 129-03-3, Cyproheptadine 361-37-5 74050-98-9, Ketanserin 135159-51-2, Anplag 147536-97-8, Bosentan 168626-94-6, YM087
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antimigratory compound, composition further containing; N-Ph-2-pyrimidine compds.
inhibiting platelet derived growth factor receptor for **treatment** of graft failure)

IT 50-78-2, Aspirin 58-32-2, Dipyridamole 55142-85-3, Ticlopidine 73963-72-1, Cilostazol 113665-84-2, Clopidogrel 143653-53-6, Abciximab 144494-65-5, Tirofiban 188627-80-7, Eptifibatide
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiplatelet agent, composition further containing; N-Ph-2-pyrimidine compds.
inhibiting platelet derived growth factor receptor for **treatment** of graft failure)

IT 106096-93-9, Basic fibroblast growth factor 106096-93-9D, Basic fibroblast growth factor, conjugates with saporin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antiproliferative antibody to, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 33069-62-4, Taxol 53123-88-9, Rapamycin 97322-87-7, Troglitazone
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(antiproliferative compound, composition further containing; N-Ph-2-pyrimidine
compds. **inhibiting** platelet derived growth factor receptor
for **treatment** of graft failure)

IT 50-28-2, 17β-Estradiol, biological studies 145-63-1, Suramin 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82834-16-0, Perindopril 85441-61-8, Quinapril 87333-19-5, Ramipril 88768-40-5, Cilazapril 93957-54-1, Fluvastatin 98048-97-6, Fosinopril 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiproliferative compds., composition further containing; N-Ph-2-pyrimidine
compds. **inhibiting** platelet derived growth factor receptor
for **treatment** of graft failure)

IT 9002-84-0, Polytetrafluoroethylene
RL: TEM (Technical or engineered material use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(graft in vascular access for hemodialysis; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 90698-26-3, p70 S6 Kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunohistochem. staining in failed human AV grafts; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 53-03-2, Prednisone 59-02-9, α-Tocopherol 59-05-2, Methotrexate 83-43-2, Methylprednisolone 305-03-3, Chlorambucil 446-86-6, Azathioprine 59865-13-3, Cyclosporine 128794-94-5, Mycophenolate mofetil 162359-56-0, FTY720
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(immunosuppressant, composition further containing; N-Ph-2-pyrimidine compds.
inhibiting platelet derived growth factor receptor for **treatment** of graft failure)

IT 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**, as angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 386705-49-3, VEGFR kinase
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**inhibitor**, as angiogenesis **inhibitor**, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 9028-06-2, Prolyl hydroxylase 68651-95-6, Procollagen C-proteinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**, as antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 58-64-0, 5'-ADP, biological studies **9036-21-9**, Phosphodiesterase III

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**, antiplatelet agent, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 101463-26-7, PDGFR tyrosine kinase
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**inhibitors**, antiproliferative and antifibrotic compds., composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 9015-82-1, Angiotensin-converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**, antiproliferative compds., composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 9028-35-7, NADPH-hydroxymethylglutaryl-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**, statins, antiproliferative compds., composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 140208-23-7, Plasminogen activator **inhibitor**-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(promoter, agent **inhibiting** activation of, as antifibrotic compound, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 58-61-7, Adenosine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reuptake **inhibitors**, antiplatelet agent, composition further containing; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

IT 115926-52-8, PI3 Kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(signaling pathway upregulated in failed human AV grafts; N-Ph-2-pyrimidine compds. **inhibiting** platelet derived growth factor receptor for **treatment** of graft failure)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2003:173603 HCAPLUS Full-text
DOCUMENT NUMBER: 138:205042
TITLE: Preparation of alkyne-aryl 1,8-naphthyridin-4(1H)ones as **phosphodiesterase-4** inhibitors
INVENTOR(S): Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte, Sebastien; Friesen, Richard
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
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LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018579	A1	20030306	WO 2002-CA1324	20020827 <--

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CA 2456817	A1	20030306	CA 2002-2456817		20020827 <--
AU 2002322940	A1	20030310	AU 2002-322940		20020827 <--
EP 1436290	A1	20040714	EP 2002-754079		20020827 <--
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BR 2002012042	A	20040817	BR 2002-12042		20020827 <--
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JP 2005508313	T	20050331	JP 2003-523241		20020827 <--
CN 1639161	A	20050713	CN 2002-821327		20020827 <--
NZ 530931	A	20051223	NZ 2002-530931		20020827 <--
ZA 2004000952	A	20041022	ZA 2004-952		20040205 <--
US 2005070569	A1	20050331	US 2004-487047		20040217 <--
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NO 2004001293	A	20040527	NO 2004-1293		20040326 <--
PRIORITY APPLN. INFO.:			US 2001-316093P	P	20010829 <--
			WO 2002-CA1324	W	20020827 <--

OTHER SOURCE(S): MARPAT 138:205042

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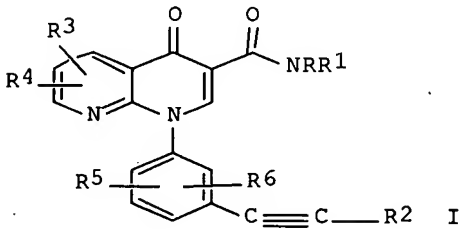

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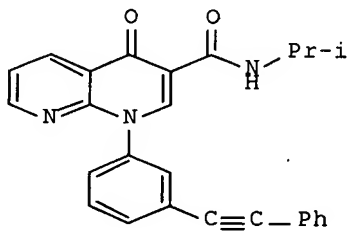

II

AB Alkyne-aryl 1,8-naphthyridin-4(1H)ones of formula I [R = H, alkyl, cycloalkyl; R1 = H, alkyl, cycloalkyl, alkoxy, acyl, Ph, heteroaryl, etc.; R2 = H, (substituted) Ph, pyridyl, pyrimidinyl, indolyl, quinolinyl, thienyl, etc. and oxides thereof; R3-R6 = H, halo, alkyl, alkoxy, nitro, CN, etc.] are prepared as phosphodiesterase 4 inhibitors useful in the treatment of asthma and inflammation. Thus, II was prepared from Et 2-chloronicotinoyl acetate, 3-bromoaniline, isopropylamine and phenylacetylene. The prepared compds. inhibited the hydrolysis of cAMP with IC50 of 0.1 nM to 90.0 nM.

IC ICM C07D471-04
ICS C07D519-00; A61K031-435

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT Inflammation

(Crohn's disease; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Intestine, disease
(Crohn's; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Respiratory distress syndrome
(adult; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Allergy
Inflammation
Nose, disease
(allergic rhinitis; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Inflammation
Spinal column, disease
(ankylosing spondylitis; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Dermatitis
(atopic; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Bronchi, disease
Inflammation
(chronic bronchitis; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Inflammation
Kidney, disease
(chronic glomerulonephritis; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Lung, disease
(chronic obstructive pulmonary disease; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Abdomen, disease
(colic; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Mental and behavioral disorders
(depression; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Granuloma
(eosinophilic; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Transplant and Transplantation
(graft-vs.-host reaction; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Injury
(head and neck; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Reperfusion
(injury, brain; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Head and Neck, disease
(injury; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Inflammation
(neurogenic; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT Respiratory distress syndrome
(newborn; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Allergy
Allergy inhibitors
Alzheimer's disease
Anti-inflammatory agents
Antiasthmatics
Asthma
Atherosclerosis
Cachexia
Cough
Human
Inflammation
Memory disorders
Multiple sclerosis
Neoplasm
Osteoarthritis
Pain
Parkinson's disease
Psoriasis
Rheumatoid arthritis
Sepsis
Transplant rejection
Urticaria
(preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Skin, disease
(proliferative; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Arthritis
(psoriatic arthritis; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Brain
(reperfusion injury; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Injury
(reperfusion, brain; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT **Artery, disease**
(**restenosis**; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Gastric acid
(secretion; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Shock (circulatory collapse)
(septic; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Spinal cord, disease
(trauma; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Inflammation
Intestine, disease
(ulcerative colitis; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT Mental and behavioral disorders
(unipolar depression; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)
IT **9036-21-9, Phosphodiesterase 4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT 500355-39-5P 500355-43-1P
RL: **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT 500355-37-3P 500355-38-4P 500355-40-8P 500355-41-9P 500355-42-0P
500355-44-2P 500355-45-3P 500355-46-4P 500355-47-5P 500355-48-6P
500355-49-7P 500355-50-0P 500355-51-1P 500355-52-2P 500355-53-3P
500355-54-4P 500355-55-5P 500355-56-6P 500355-57-7P 500355-58-8P
500355-59-9P 500355-60-2P 500355-61-3P 500355-62-4P 500355-63-5P
500355-64-6P 500355-65-7P 500355-66-8P 500355-67-9P 500355-68-0P
500355-69-1P 500355-70-4P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT 67-64-1, Acetone, reactions 75-31-0, Isopropylamine, reactions
115-19-5, 2-Methyl-3-butyn-2-ol 127-66-2, 2-Phenyl-3-butyn-2-ol
288-47-1, Thiazole 536-74-3, Phenylacetylene 589-87-7,
4-Bromoiodobenzene 591-19-5, 3-Bromoaniline 624-28-2,
2,5-Dibromopyridine 626-05-1, 2,6-Dibromopyridine 626-55-1,
3-Bromopyridine 684-16-2, Hexafluoroacetone 765-30-0, Cyclopropylamine
1066-54-2, Trimethylsilylacetylene 1072-97-5, 5-Bromo-2-aminopyridine
1692-25-7, Pyridine-3-boronic acid 1945-84-2, 2-Ethynylpyridine
2510-22-7, 4-Ethynylpyridine 2510-23-8, 3-Ethynylpyridine 3234-64-8,
1,1-Diethylpropargylamine 5332-24-1, 3-Bromoquinoline 5370-25-2,
2-Acetyl-5-bromothiophene 6746-94-7, Cyclopropylacetylene 17356-19-3,
1-Ethynylcyclopentanol 20986-40-7, Ethyl 5-bromonicotinate 22615-00-5,
3-Bromoquinoline N-oxide 27374-25-0 66572-56-3, 2-Bromoisonicotinic acid 220731-02-2, Ethyl 2-chloronicotinoyl acetate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

IT 477251-77-7P 477251-78-8P 477251-79-9P 477251-96-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alkyne-aryl naphthyridinones as **phosphodiesterase 4** inhibitors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 20 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:22685 HCAPLUS Full-text
DOCUMENT NUMBER: 138:73184
TITLE: Preparation of substituted 8-arylquinoline **phosphodiesterase-4** (PDE4) inhibitors
INVENTOR(S): Dube, Daniel; Girard, Yves; MacDonald, Dwight; Mastracchio, Anthony; Gallant, Michel; Lacombe, Patrick; Deschenes, Denis
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002118	A1	20030109	WO 2002-CA953	20020626 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2450686	A1	20030109	CA 2002-2450686	20020626 <--
AU 2002344885	A1	20030303	AU 2002-344885	20020626 <--
EP 1404330	A1	20040407	EP 2002-742600	20020626 <--
EP 1404330	B1	20050601		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005501822	T	20050120	JP 2003-508357	20020626 <--
AT 296630	T	20050615	AT 2002-742600	20020626 <--
ES 2242036	T3	20051101	ES 2002-2742600	20020626 <--
US 2004162314	A1	20040819	US 2003-478791	20031125 <--
US 6919353	B2	20050719		

PRIORITY APPLN. INFO.:	US 2001-301220P	P	20010627 <--
	US 2001-303472P	P	20010706 <--
	WO 2002-CA953	W	20020626 <--

OTHER SOURCE(S): MARPAT 138:73184
ED Entered STN: 10 Jan 2003
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 8-Arylquinolines (shown as I; variables defined below; e.g. both enantiomers of 4-hydroxy-1-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin- 8-yl]phenyl]-2-(4-methanesulfonylphenyl)-4-methylpentan-3-one) wherein the aryl group at the 8-position contains a meta two atom bridge to an optionally substituted Ph or pyridyl group, are PDE4 inhibitors useful to treat asthma, chronic bronchitis, chronic obstructive pulmonary disease, arthritis, respiratory distress syndrome, allergic rhinitis, neurogenic inflammation, pain, rheumatoid arthritis, and other diseases. R1-R7 and Ar are as in claim 1. For I: Ar is Ph, pyridinone, pyridyl, or pyridyl N-oxide, optionally substituted with 1-5 independent -C1-6-alkyl, -OH, -CN, halogen, -CF3, -(C0-6-alkyl)-SOn-(C1-6-alkyl), -(C0-6-alkyl)-SOn-NH- (C1-6-alkyl) or 5-membered heteroaryl ring containing 1-4 heteroatoms = O, S or N, wherein the 5-membered-ring is optionally substituted. R1 is H, halogen; or a -C1-6-alkyl, -cycloC3-6alkyl, -C1-6-alkenyl, -C0-4alkyl-C(O)-C0-4alkyl, -C1-6-alkoxy, aryl, heteroaryl, -CN, -heterocycloC3-6-alkyl, -amino, -C1-6-alkylamino, -(C1-6-alkyl)(C1-6- alkyl)amino, -C1-6-alkyl(oxy)C1-6-alkyl, -C(O)NH(aryl), -C(O)NH(heteroaryl), -SOnNH(aryl), -SOnNH(heteroaryl), -SOnNH(C1-6-alkyl), -C(O)N(C0-6alkyl)(C0-6-alkyl), -NH-SOn-(C1-6-alkyl), -carbamoyl, -(C1-6-alkyl)-O-C(CN)dialkylamino, or -(C0-6-alkyl)-SOn-(C1-6-alkyl) group, wherein any of the groups is optionally substituted with = 1-5 substituents. R2, R3, R6, and R7 = H, halogen, hydroxy, -C1-6-alkyl, or -C1-6-alkoxy, wherein the alkyl and alkoxy are optionally substituted independently with 1-3 halogen or OH; R4 is H, halogen, -CN, Ph, oxadiazolyl, or -C(O)-O-C0-6alkyl, wherein the alkyl and

latter three possibilities are optionally substituted. R5 is H, hydroxy, -CN; or a -C1-6-alkyl, -C(O)C1-6alkyl, -C(O)aryl, -C(O)pyridyl, -C(O)-O-C0-6-alkyl, -C(O)-C3-7-cycloalkyl, -C1-6-alkyl-C3-7cycloalkyl, -C1-6-alkyl(C3-7-cycloalkyl)2, -C1-6-alkylaryl, -C(O)-N(C0-6alkyl)2, -SOnaryl, -SOn-C1-6-alkyl, -SOn-C3-7-cycloalkyl, -SOn-N(C0-6-alkyl)2, -P(O)(C1-6-alkyl)2, -P(O)(C1-6-alkoxy)2, Ph, pyridyl, -SOnimidazolyl, -SOnthiazolyl, 5-membered heteroaryl ring containing 1-4 heteroatoms = O, S or N or oxoisoxaphosphinanyl group, any of which group optionally substituted; or R5 and R6 form :O; or R6 and R3 form -CH2- or -O-; and n is 0-2. Although the methods of preparation are not claimed, >100 example prepns. are included. The IC50 values for PDE4 inhibition of Examples 1-113 generally are 0.02-26 μM as measured using LPS and FMLP-induced TNF-α and LTB4 assays in human whole blood. I were tested for effects on an IgE-mediated allergic pulmonary inflammation induced by inhalation of antigen by sensitized guinea pigs;. Administration of I (0.001-10 mg/kg i.p. or p.o.), up to three times during the 48 h following antigen challenge, lead to a significant reduction in the eosinophilia and the accumulation of other inflammatory leukocytes. There was also less inflammatory damage in the lungs of animals treated with I. Compds. which inhibit the hydrolysis of cAMP to AMP by the type-IV cAMP-specific phosphodiesterases were screened in a 96-well plate format; IC50 values of I generally ranged 0.1-25 nM.

IC ICM A61K031-47
ICS C07D215-12; C07D401-10; C07D405-10; C07D417-12; C07F009-60; C07F009-6571; C07D403-10; C07D413-10; C07D417-10; C07D405-14; A61P011-06; A61P029-00; A61P017-06

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST arylquinoline prepn **phosphodiesterase 4** inhibitor therapeutic use; quinoline aryl prepn **phosphodiesterase 4** inhibitor therapeutic use

IT Corticosteroids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combined with substituted 8-arylquinoline PDE4 inhibitors for various therapeutic uses)

IT Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Antiarthritics
Antiasthmatics
Antidepressants
Antidiabetic agents
Antirheumatic agents
Antitumor agents
Arthritis
Asthma
Atherosclerosis
Cachexia
Cognition enhancers
Cough
Diabetes insipidus
Memory disorders
Multiple sclerosis
Neoplasm
Osteoarthritis
Pain
Parkinson's disease
Psoriasis
Rheumatoid arthritis
Transplant rejection

Urticaria
(preparation of substituted 8-arylquinoline PDE4 inhibitors with various therapeutic uses)

IT **Artery, disease**
(**restenosis**; preparation of substituted 8-arylquinoline PDE4 inhibitors with various therapeutic uses)

IT 481679-76-9P 481679-77-0P, 1-(4-Fluorophenyl)-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propan-1-one 481679-81-6P, 1-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-4,4-dimethylpentan-3-one 481679-82-7P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propionic acid methyl ester 481679-84-9P, 1-Cyclopropyl-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propan-1-one 481679-86-1P, 5-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-4-(4-methanesulfonylphenyl)-2,3-dimethylpentane-2,3-diol 481679-87-2P, 1-Cyclopropyl-2-fluoro-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propan-1-one 481679-95-2P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methylsulfanylphenyl)propan-1-ol 481679-97-4P, 2-Hydroxy-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propionic acid ethyl ester 481680-00-6P, 1-(4-Fluorophenyl)-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-2-methylpropan-1-one 481680-08-4P, 2-Fluoro-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methylsulfanylphenyl)propionic acid ethyl ester 481680-09-5P, 2-Fluoro-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propionic acid ethyl ester 481680-20-0P, 2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethanone 481680-24-4P, 2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethanol 481680-25-5P, 4-[2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethylsulfanyl]benzoic acid ethyl ester 481680-27-7P, 2-[4-[2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethanesulfonyl]phenyl]propan-2-ol 481680-33-5P, 6-(1-Methanesulfonyl-1-methylethyl)-8-[3-[2-(4-methanesulfonylphenyl)-2-(1-methyl-1H-imidazole-2-sulfonyl)ethyl]phenyl]quinoline 481680-36-8P, 4-Hydroxy-2-[4-(1-hydroxy-1-methylethyl)phenyl]-1-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-4-methylpentan-3-one 481680-40-4P, 8-[3-[2-(5,5-Dimethyl-2-oxo-2λ5-[1,3,2]dioxaphosphinan-2-yl)-2-(4-methanesulfonylphenyl)ethyl]phenyl]-6-(1-methanesulfonyl-1-methylethyl)quinoline 481680-44-8P, 2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethanesulfonic acid dimethylamide 481680-46-0P, 8-[3-[1-(4-Chlorophenyl)-2-pyridin-4-ylethyl]phenyl]-6-isopropylquinoline 481680-49-3P, 3-(4-Chlorophenyl)-3-[3-(6-isopropylquinolin-8-yl)phenyl]-2-pyridin-4-ylpropionic acid ethyl ester 481680-51-7P, 8-[3-[1-(4-Chlorophenyl)-2-pyridin-4-ylethyl]phenyl]quinoline 481680-54-0P, 6-Isopropyl-8-[3-(2-pyridin-4-ylethyl)phenyl]quinoline 481680-56-2P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-pyridin-4-ylpropionic acid ethyl ester 481680-58-4P, 4-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-methyl-3-pyridin-4-ylbutan-2-ol 481680-60-8P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-pyridin-4-ylbutyric acid ethyl ester 481680-63-1P, 2-Pyridin-4-yl-3-[3-(6-pyridin-4-ylmethylquinolin-8-yl)phenyl]propionic acid ethyl ester 481680-66-4P 481680-69-7P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-(4-methanesulfonylphenyl)propionitrile 481680-76-6P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-(4-methanesulfonylphenyl)propionic acid methyl ester 481680-87-9P, 2-[3-(6-Isopropylquinolin-8-yl)phenyl]-3-(4-

methanesulfonylphenyl)propionic acid methyl ester 481680-88-0P, 2-[3-(6-Isopropylquinolin-8-yl)phenyl]-3-(4-methanesulfonylphenyl)propionic acid
RL: **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of substituted 8-arylquinoline **phosphodiesterase-4** (PDE4) inhibitors)

IT 481679-78-1P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-1-p-tolylpropan-1-one 481679-79-2P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-1-pyridin-2-ylpropan-1-one 481679-80-5P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-1-pyridin-3-ylpropan-1-one 481679-83-8P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propionic acid 481679-88-3P 481679-89-4P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-1-phenylpropan-1-one 481679-94-1P, 4-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-3-(4-methanesulfonylphenyl)butan-2-one 481679-96-3P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propan-1-ol 481679-99-6P, 2-(4-Fluorophenyl)-4-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-3-(4-methanesulfonylphenyl)butan-2-ol 481680-01-7P, 1-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-2,4,4-trimethylpentan-3-one 481680-02-8P, 1-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-4,4-dimethylpentan-3-ol 481680-03-9P, 1-(4-Fluorophenyl)-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propan-1-ol 481680-04-0P, 2-(4-Fluorophenyl)-4-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-3-(4-methanesulfonylphenyl)-3-methylbutan-2-ol 481680-05-1P, 4-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-3-(4-methanesulfonylphenyl)-2-methylbutan-2-ol 481680-06-2P, 1,1,1-Trifluoro-4-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-3-(4-methanesulfonylphenyl)butan-2-ol 481680-10-8P, 2-Fluoro-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propan-1-ol 481680-11-9P 481680-12-0P, 1-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-3-methylbutane-2,3-diol 481680-13-1P, 2-Fluoro-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propionic acid 481680-14-2P, 3-Ethyl-2-fluoro-1-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)pentan-3-ol 481680-15-3P 481680-16-4P, 4-[2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethyl]-4,5,5-trimethyl-[1,3]dioxolan-2-one 481680-17-5P, 5-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-4-(4-methanesulfonylphenyl)-2-methylpentane-2,3-diol 481680-18-6P, 2-Fluoro-4-hydroxy-1-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-4-methylpentan-3-one 481680-19-7P, 4-Hydroxy-1-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-4-methyl-2-(4-methylsulfanylphenyl)pentan-3-one 481680-26-6P, 2-[4-[2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethylsulfanyl]phenyl]propan-2-ol 481680-28-8P, 2-[4-[1-Fluoro-2-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethanesulfonyl]phenyl]propan-2-ol 481680-29-9P 481680-30-2P, 8-[3-[2-Methanesulfonyl-2-(4-methanesulfonylphenyl)ethyl]phenyl]-6-(1-methanesulfonyl-1-methylethyl)quinoline 481680-31-3P, 8-[3-[2-Ethanesulfonyl-2-fluoro-2-(4-

methanesulfonylphenyl)ethyl]phenyl]-6-(1-methanesulfonyl-1-methylethyl)quinoline 481680-34-6P, 8-[3-[2-Fluoro-2-(4-methanesulfonylphenyl)-2-(1-methyl-1H-imidazole-2-sulfonyl)ethyl]phenyl]-6-(1-methanesulfonyl-1-methylethyl)quinoline 481680-35-7P, 8-[3-[2-Fluoro-2-(4-methanesulfonylphenyl)-2-(thiazole-2-sulfonyl)ethyl]phenyl]-6-(1-methanesulfonyl-1-methylethyl)quinoline 481680-37-9P, 4-[4-(1-Hydroxy-1-methylethyl)phenyl]-5-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-methylpentane-2,3-diol 481680-38-0P, 2-[4-[1-Methanesulfonyl-2-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]ethyl]phenyl]propan-2-ol 481680-39-1P, [2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethyl]phosphonic acid dimethyl ester 481680-41-5P, [1-Fluoro-2-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethyl]phosphonic acid dimethyl ester 481680-42-6P, 8-[3-[2-(5,5-Dimethyl-2-oxo-2λ5-[1,3,2]dioxaphosphinan-2-yl)-2-fluoro-2-(4-methanesulfonylphenyl)ethyl]phenyl]-6-(1-methanesulfonyl-1-methylethyl)quinoline 481680-43-7P 481680-45-9P, 1-Fluoro-2-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)ethanesulfonic acid dimethylamide 481680-50-6P, 8-[3-[1-(4-Chlorophenyl)-2-(1-oxopyridin-4-yl)ethyl]phenyl]-6-isopropylquinoline 481680-53-9P, 8-[3-[1-(4-Chlorophenyl)-2-(1-oxopyridin-4-yl)ethyl]phenyl]quinoline 481680-55-1P, 6-Isopropyl-8-[3-[2-(1-oxopyridin-4-yl)ethyl]phenyl]quinoline 481680-57-3P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-pyridin-4-ylpropan-1-ol 481680-59-5P, 4-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-methyl-3-(1-oxopyridin-4-yl)butan-2-ol 481680-61-9P, 4-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-methyl-3-pyridin-4-ylpentan-2-ol 481680-62-0P, 4-(4-Chlorophenyl)-4-[3-(6-isopropylquinolin-8-yl)phenyl]-2-methyl-3-pyridin-4-ylbutan-2-ol 481680-64-2P, 2-Methyl-3-pyridin-4-yl-4-[3-(6-pyridin-4-ylmethylquinolin-8-yl)phenyl]butan-2-ol 481680-65-3P, 8-[3-[1-(4-Chlorophenyl)-2-pyridin-4-ylethyl]phenyl]-6-pyridin-4-ylmethylquinoline 481680-67-5P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-pyridin-4-ylpropionitrile 481680-71-1P, 6-Isopropyl-8-[3-[2-(4-methanesulfonylphenyl)-2-(1H-tetrazol-5-yl)ethyl]phenyl]quinoline 481680-72-2P, 3-[3-[6-(Cyanodimethylmethyl)quinolin-8-yl]phenyl]-N-isopropyl-2-(4-methanesulfonylphenyl)propionamide 481680-73-3P 481680-75-5P, 6-(1-Methanesulfonyl-1-methylethyl)-8-[3-[2-(4-methanesulfonylphenyl)-2-(3-methyl-[1,2,4]oxadiazol-5-yl)ethyl]phenyl]quinoline 481680-78-8P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-(4-methanesulfonylphenyl)propionic acid 481680-79-9P, 6-Isopropyl-8-[3-[2-(4-methanesulfonylphenyl)-2-(3-methyl-[1,2,4]oxadiazol-5-yl)ethyl]phenyl]quinoline 481680-80-2P, 3-(2-Cyanophenyl)-2-[3-(6-isopropylquinolin-8-yl)phenyl]propionic acid methyl ester 481680-81-3P, 3-(3-Cyanophenyl)-2-[3-(6-isopropylquinolin-8-yl)phenyl]propionic acid methyl ester 481680-82-4P, 3-(4-Cyanophenyl)-2-[3-(6-isopropylquinolin-8-yl)phenyl]propionic acid methyl ester 481680-83-5P, 3-(2-Chloro-4-fluorophenyl)-2-[3-(6-isopropylquinolin-8-yl)phenyl]propionic acid methyl ester 481680-84-6P, 2-[3-(6-Isopropylquinolin-8-yl)phenyl]-3-[4-(1,2,3-thiadiazol-5-yl)phenyl]propionic acid methyl ester 481680-85-7P, 2-[3-(6-Isopropylquinolin-8-yl)phenyl]-3-pyridin-4-ylpropionic acid methyl ester 481680-86-8P, 2-[3-(6-Isopropylquinolin-8-yl)phenyl]-3-phenylpropionic acid methyl ester 481680-89-1P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-4-(4-methanesulfonylphenyl)-2-methylbutan-2-ol 481680-90-4P, N-Isopropyl-2-[3-(6-isopropylquinolin-8-yl)phenyl]-3-(4-methanesulfonylphenyl)propionamide 481680-91-5P, 6-Isopropyl-8-[3-[2-(4-methanesulfonylphenyl)-1-(3-methyl-[1,2,4]oxadiazol-5-yl)ethyl]phenyl]quinoline 481680-92-6P, 2-[3-(6-Isopropylquinolin-8-yl)phenyl]-3-(4-methanesulfonylphenyl)propionitrile 481680-93-7P, 2-[3-(6-Isopropylquinolin-8-yl)phenyl]-3-pyridin-3-ylpropionic acid methyl ester 481680-94-8P, 2-[3-(6-Isopropylquinolin-8-yl)phenyl]-3-(4-

methanesulfonylphenyl)-2-methylpropionic acid methyl ester 481680-95-9P, 2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)cyclopropanecarboxylic acid 481680-99-3P, [2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)cyclopropyl]methanol 481681-00-9P, 2-[2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)cyclopropyl]propan-2-ol 481681-01-0P, 8-[4-Fluoro-3-[2-(4-methanesulfonylphenyl)ethyl]phenyl]-6-isopropylquinoline 481681-06-5P, 8-[2-Fluoro-5-[2-(4-methanesulfonylphenyl)ethyl]phenyl]-6-isopropylquinoline 481681-07-6P 481681-08-7P, 2-(4-Cyclopropanesulfonylphenyl)-4-hydroxy-1-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-4-methylpentan-3-one 481681-09-8P, 4-Ethyl-4-hydroxy-1-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)hexan-3-one 481681-10-1P, 8-[3-[2,2-Bis(4-chlorophenyl)cyclopropyl]phenyl]-6-isopropylquinoline 481681-12-3P, 8-[3-[2,2-Bis(4-methanesulfonylphenyl)cyclopropyl]phenyl]-6-isopropylquinoline 481681-13-4P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-pyridin-4-yloxirane-2-carbonitrile 481681-14-5P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-(1-oxopyridin-4-yl)oxirane-2-carbonitrile 481681-16-7P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-pyridin-2-yloxirane-2-carboxylic acid ethyl ester 481681-17-8P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-(1-oxopyridin-2-yl)oxirane-2-carboxylic acid ethyl ester 481681-18-9P 481681-19-0P 481681-20-3P 481681-21-4P 481681-22-5P 481681-23-6P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of substituted 8-arylquinoline **phosphodiesterase-4** (PDE4) inhibitors)

IT 9028-35-7
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitors, statins; combined with substituted 8-arylquinoline PDE4 inhibitors for various therapeutic uses)

IT **9036-21-9**, PDE4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of substituted 8-arylquinoline PDE4 inhibitors)

IT 60-56-0, 2-Mercapto-N-methylimidazole 75-31-0, Isopropylamine, reactions 75-89-8, 2,2,2-Trifluoroethanol 75-97-8, Pinacolone 90-98-2, Bis(4-chlorophenyl)methanone 96-22-0, 3-Pentanone 100-44-7, Benzyl chloride, reactions 100-58-3, Phenylmagnesium bromide 100-59-4, Phenylmagnesium chloride 100-68-5, Thioanisole 104-95-0, 4-Bromothioanisole 106-53-6, 4-Bromothiophenol 108-18-9, Diisopropylamine 115-22-0, 3-Hydroxy-3-methylbutan-2-one 122-00-9 126-30-7, 2,2-Dimethyl-1,3-propanediol 350-03-8, 3-Acetylpyridine 403-42-9 765-43-5, 1-Cyclopropylethanone 873-77-8, 4-Chlorophenylmagnesium bromide 874-87-3, 4-Methylthiobenzyl chloride 932-77-4, 3-Bromobenzyl chloride 1122-62-9, 2-Acetylpyridine 1878-67-7, 3-Bromophenylacetic acid 3099-31-8, 3-Picolyl chloride 3132-99-8, 3-Bromobenzaldehyde 3446-89-7, 4-Methylthiobenzaldehyde 4755-77-5, Ethyloxalyl chloride 5685-05-2, 2-Mercaptothiazole 5798-75-4, Ethyl 4-bromobenzoate 10445-91-7, 4-Picolyl chloride 13121-99-8, 4-Pyridinylacetonitrile 16188-55-9, (4-Methylsulfanylphenyl)acetic acid 16567-18-3, 8-Bromoquinoline 17201-43-3, 4-Cyanobenzyl bromide 22115-41-9, 2-Cyanobenzyl bromide 23719-80-4, Cyclopropylmagnesium bromide 28188-41-2, 3-Cyanobenzyl bromide 28276-32-6, Ethyl 4-mercaptobenzoate 40517-43-9, 4-Methanesulfonylbenzyl chloride 45767-66-6, 2-Chloro-4-fluorobenzyl bromide 54401-85-3, Ethyl 4-pyridinylacetate 56066-91-2, 4-Carboxymethylbenzyl chloride 73183-34-3, Diboron pinacol ester 77771-03-0, 3-Bromo-4-fluorobenzyl alcohol 87199-15-3,

3-(Hydroxymethyl)phenylboronic acid 87199-16-4, 3-Formylphenylboronic acid 90536-66-6, (4-Methanesulfonylphenyl)acetic acid 154586-22-8, 5-(4-Bromomethylphenyl)-[1,2,3]thiadiazole 159925-41-4, 8-Bromo-6-isopropylquinoline 159925-47-0, 6-Bromomethyl-8-bromoquinoline 188582-62-9, 4-Bromo-2-fluorobenzyl alcohol 191230-34-9, 8-Bromo-6-[(4-pyridinyl)methyl]quinoline
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted 8-arylquinoline **phosphodiesterase-4** (PDE4) inhibitors)

IT 1143-92-6P, Diazobis(4-chlorophenyl)methane 2077-19-2P, 2-(4-Bromophenyl)propan-2-ol 5335-84-2P, 4-Bromobenzene disulfide 5463-11-6P, [Bis(4-chlorophenyl)methylene]hydrazine 19849-26-4P, 3-Ethyl-3-hydroxypentan-2-one 25025-07-4P, (4-Methanesulfonylphenyl)acetonitrile 36187-57-2P, 1-(4-Fluorophenyl)-2-(4-methylsulfanylphenyl)ethanone 40061-50-5P, 2-(4-Methanesulfonylphenyl)-1-pyridin-3-ylethanone 40517-47-3P, 2-(4-Methanesulfonylphenylmethanesulfonyl)-1-methyl-1H-imidazole 62936-31-6P, Ethyl α-oxo-4-methylthiophenylacetate 63084-99-1P, Bis(4-methylsulfanylphenyl)methanone 70290-37-8P, (4-Methylsulfanylphenyl)acetic acid methyl ester 93629-02-8P, (4-Methanesulfonylphenyl)methanethiol 132470-25-8P, 1-(4-Fluorophenyl)-2-(4-methanesulfonylphenyl)ethanone 139278-57-2P, (4-Methanesulfonylbenzyl)phosphonic acid dimethyl ester 141971-69-9P, Bis(4-methylsulfanylphenyl)methanol 150529-73-0P, (3-Bromophenyl)acetic acid methyl ester 160446-22-0P, 4-[(Methanesulfonyl)methyl]benzoic acid methyl ester 163295-77-0P, (4-Methanesulfonylphenyl)methanesulfonyl chloride 300355-18-4P, (4-Methanesulfonylphenyl)acetic acid methyl ester 346629-72-9P, Bis(4-methanesulfonylphenyl)methanone 346629-82-1P, (E)-3-(3-Bromophenyl)-2-[4-(methylsulfonyl)phenyl]-2-propenoic acid 346629-84-3P, 5-(4-Methanesulfonylbenzyl)-3-methyl-[1,2,4]oxadiazole 346629-87-6P, 8-(3-Bromomethylphenyl)-6-isopropylquinoline 346629-94-5P, (E)-N-Isopropyl-3-(3-bromophenyl)-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-97-8P, 8-Bromo-6-[(methanesulfonyl)methyl]quinoline 346629-99-0P, 8-Bromo-6-(1-methanesulfonyl-1-methylethyl)quinoline 346630-00-0P, (8-Bromoquinolin-6-yl)acetonitrile 346630-01-1P, 2-(8-Bromoquinolin-6-yl)-2-methylpropionitrile 346630-03-3P, 3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]benzaldehyde 411229-63-5P, 1-Bromo-4-cyclopropylsulfanylbenzene 478375-42-7P, [3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)phenyl]acetic acid methyl ester 481679-37-2P, 8-(3-Bromomethylphenyl)-6-(1-methanesulfonyl-1-methylethyl)quinoline 481679-38-3P, [3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]methanol 481679-39-4P, [3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]methanol O-methanesulfonate 481679-40-7P, 3-(6-Isopropylquinolin-8-yl)benzaldehyde 481679-41-8P, [3-(6-Isopropylquinolin-8-yl)phenyl]acetic acid methyl ester 481679-42-9P, [3-(6-Isopropylquinolin-8-yl)phenyl]acetonitrile 481679-43-0P, 2-[8-(3-Bromomethylphenyl)quinolin-6-yl]-2-methylpropionitrile 481679-44-1P, Hydroxy(4-methylsulfanylphenyl)acetic acid ethyl ester 481679-45-2P, Fluoro(4-methylsulfanylphenyl)acetic acid ethyl ester 481679-46-3P, N-Isopropyl-2-(4-methanesulfonylphenyl)acetamide 481679-47-4P, 3-Hydroxy-3-methyl-1-(4-methylsulfanylphenyl)butan-2-one 481679-48-5P, 3-Hydroxy-1-(4-methanesulfonylphenyl)-3-methylbutan-2-one 481679-49-6P, 2-(4-Methanesulfonylphenyl)-1-p-tolylethanone 481679-50-9P, 2-(4-Methanesulfonylphenyl)-1-pyridin-2-ylethanone 481679-51-0P, 1-(4-Methanesulfonylphenyl)-3,3-dimethylbutan-2-one 481679-52-1P, 1-Cyclopropyl-2-(4-methanesulfonylphenyl)ethanone 481679-53-2P, 1-(4-Fluorophenyl)-2-(4-methanesulfonylphenyl)propan-1-one 481679-54-3P, 4-(4-Methanesulfonylphenyl)-2,2-dimethylpentan-3-one 481679-55-4P, 3-Hydroxy-1-[4-(1-hydroxy-1-methylethyl)phenyl]-3-methylbutan-2-one 481679-56-5P, 3-Ethyl-3-hydroxy-1-(4-methanesulfonylphenyl)pentan-2-one

481679-57-6P, 1-Methanesulfonyl-4-[(methanesulfonyl)methyl]benzene
481679-58-7P, 1-(Fluoro(methanesulfonyl)methyl)-4-methanesulfonylbenzene
481679-59-8P, 1-[(Cyclopropanesulfonyl)methyl]-4-methanesulfonylbenzene
481679-60-1P, (4-Methylsulfanylphenyl)methanethiol disulfide
481679-61-2P, 1-[(Cyclopropylsulfanyl)methyl]-4-methylsulfanylbenzene
481679-62-3P, 1-[(Ethanesulfonyl)methyl]-4-methanesulfonylbenzene
481679-63-4P, 1-[(Ethylsulfanyl)methyl]-4-methanesulfonylbenzene
481679-64-5P, 2-(4-Methanesulfonylbenzylsulfanyl)-1-methyl-1H-imidazole
481679-65-6P, 2-(4-Methanesulfonylphenylmethanesulfonyl)thiazole
481679-66-7P, 2-(4-[(Methanesulfonyl)methyl]phenyl)propan-2-ol
481679-67-8P, C-(4-Methanesulfonylphenyl)-N,N-dimethylmethanesulfonamide
481679-68-9P, 1-(4-Cyclopropanesulfonylphenyl)-3-hydroxy-3-methylbutan-2-one 481679-69-0P, 1-(4-Cyclopropylsulfanylphenyl)-3-hydroxy-3-methylbutan-2-one 481679-70-3P, (4-Methylsulfanylbenzyl)phosphonic acid dimethyl ester 481679-71-4P, [Fluoro(4-methanesulfonylphenyl)methyl]phosphonic acid dimethyl ester 481679-72-5P, 2-(4-Methanesulfonylbenzyl)-5,5-dimethyl-[1,3,2]dioxaphosphinane 2-oxide 481679-73-6P, (4-Methanesulfonylbenzyl)phosphonic acid 481679-74-7P, (4-Methanesulfonylbenzyl)phosphonoyl chloride 481679-75-8P, (4-Methanesulfonylbenzyl)phosphonic acid bis(2,2,2-trifluoroethyl) ester 481679-85-0P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-N-methoxy-N-methylpropionamide 481679-90-7P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methylsulfanylphenyl)propionic acid methyl ester 481679-91-8P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methylsulfanylphenyl)propionaldehyde 481679-92-9P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methylsulfanylphenyl)-1-phenylpropan-1-ol 481679-93-0P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methylsulfanylphenyl)-1-phenylpropan-1-one 481679-98-5P, 2-Hydroxy-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methylsulfanylphenyl)propionic acid ethyl ester 481680-07-3P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)propionaldehyde 481680-21-1P, (tert-Butyldimethylsilanyloxy)(4-methylsulfanylphenyl)acetonitrile 481680-22-2P, 2-(tert-Butyldimethylsilanyloxy)-3-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methylsulfanylphenyl)propionitrile 481680-23-3P, 2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methylsulfanylphenyl)ethanone 481680-32-4P, 8-[3-[2-Ethanesulfonyl-2-(4-methanesulfonylphenyl)ethyl]phenyl]-6-(1-methanesulfonyl-1-methylethyl)quinoline 481680-47-1P, (4-Chlorophenyl)[3-(6-isopropylquinolin-8-yl)phenyl]methanol 481680-48-2P, 8-[3-[Chloro(4-chlorophenyl)methyl]phenyl]-6-isopropylquinoline 481680-52-8P, 4-[2-(3-Bromophenyl)-2-(4-chlorophenyl)ethyl]pyridine 481680-68-6P, 3-(3-Bromophenyl)-2-pyridin-4-ylpropionitrile 481680-70-0P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-[4-(methylsulfonyl)phenyl]prop-2-enenitrile 481680-74-4P, 3-[3-[6-(Cyanodimethylmethyl)quinolin-8-yl]phenyl]-N-isopropyl-2-(4-methanesulfonylphenyl)acrylamide 481680-77-7P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-(4-methylsulfanylphenyl)propionic acid methyl ester 481680-96-0P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)acrylic acid 481680-97-1P, 3-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)acrylic acid methyl ester 481680-98-2P, 2-[3-[6-(1-Methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-1-(4-methanesulfonylphenyl)cyclopropanecarboxylic acid methyl ester 481681-02-1P, 4-Fluoro-3-hydroxymethylbenzeneboronic acid 481681-03-2P, [2-Fluoro-5-(6-isopropylquinolin-8-yl)phenyl]methanol 481681-04-3P, 2-Fluoro-5-(6-isopropylquinolin-8-yl)benzaldehyde 481681-05-4P, 8-[4-Fluoro-3-[2-(4-methanesulfonylphenyl)vinyl]phenyl]-6-

isopropylquinoline 481681-11-2P, 6-Isopropyl-8-(3-vinylphenyl)quinoline 481681-15-6P, 3-[3-(6-Isopropylquinolin-8-yl)phenyl]-2-pyridin-4-ylacrylonitrile
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted 8-arylquinoline **phosphodiesterase-4** (PDE4) inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 21 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:906219 HCAPLUS Full-text
DOCUMENT NUMBER: 138:4594
TITLE: Preparation of 1-biaryl-[1,8]naphthyridin-**4**-one **phosphodiesterase** IV inhibitors for treatment of asthma and inflammation
INVENTOR(S): Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte, Sebastien; Friesen, Richard; Girard, Yves; Li, Chun
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
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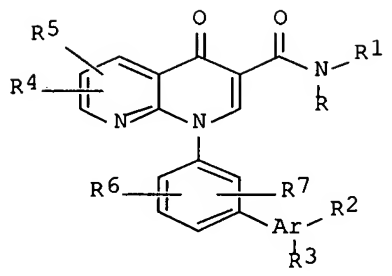
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002094823	A1	20021128	WO 2002-CA746		20020522 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2447765	A1	20021128	CA 2002-2447765		20020522 <--
AU 2002257459	A1	20021203	AU 2002-257459		20020522 <--
EP 1397359	A1	20040317	EP 2002-727127		20020522 <--
EP 1397359	B1	20050831			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004534773	T	20041118	JP 2002-591496		20020522 <--
AT 303384	T	20050915	AT 2002-727127		20020522 <--
ES 2247325	T3	20060301	ES 2002-2727127		20020522 <--
US 2003096829	A1	20030522	US 2002-154591		20020524 <--
US 6677351	B2	20040113			
PRIORITY APPLN. INFO.:			US 2001-293247P	P	20010524 <--
			WO 2002-CA746	W	20020522 <--

OTHER SOURCE(S): MARPAT 138:4594
ED Entered STN: 29 Nov 2002
GI



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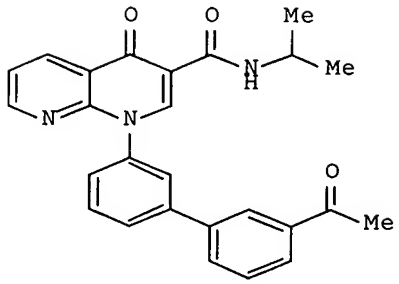

II

AB Title compds. I [wherein Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl, or heteroaryl oxides; R = H or alkyl; R1 = H or (un)substituted (cyclo)alkyl, alkoxy, alkenyl, alkynyl, heteroaryl, or heterocyclyl; R2 = H, halo, (cyclo)alkyl, alkoxy, amino, acyl, alkoxycarbonyl, alkylsulfamoyl, alkylsulfonyl, or (un)substituted Ph, heteroaryl, or heterocyclyl, etc.; R3 = H, OH, NH2, halo, (un)substituted alkyl; R4-R7 = independently H, halo, NH2, or (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors for the treatment of asthma and inflammation. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate was cyclized using NaH in THF and the resulting ester saponified to give 1-(3-bromophenyl)-1,4- dihydro-[1,8]naphthyridin-4-one-3-carboxylic acid. Amidation with isopropylamine, followed by treatment with 3-acetylphenylboronic acid in the presence of trans-PdBr2(PPh3)2 and Na2CO3 in toluene and EtOH gave II. I demonstrated PDE4 inhibitory activity by suppression of TNF-α secretion in LPS stimulated human blood with IC50 values generally ranging from 0.005 μM to 15.4 μM. In a SPA based PDE activity assay, I inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC50 values between 34.3 nM and 134.0 nM.

IC ICM C07D471-04
ICS A61K031-435; A61K031-495; A61P011-06; A61P029-00

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**

IT Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Antiarthritics
Antiasthmatics
Antibacterial agents
Antidepressants
Antidiabetic agents
Antiparkinsonian agents
Antirheumatic agents
Antitumor agents
Antitussives
Antiviral agents
Asthma
Atherosclerosis
Cachexia
Cognition enhancers
Cough
Diabetes insipidus
Fungicides
Human
Inflammation

Memory disorders
Neoplasm
Osteoarthritis
Pain
Parkinson's disease
Psoriasis
Rheumatoid arthritis
Sepsis
Skin, disease
Transplant rejection
(preparation of biarylnaphthyridinone PDE4 inhibitors by cyclization and arylation of (arylamino)(nicotinoyl)acrylates for treatment of asthma and inflammation)

IT **Artery, disease**
(**restenosis**; preparation of biarylnaphthyridinone PDE4 inhibitors by cyclization and arylation of (arylamino)(nicotinoyl)acrylates for treatment of asthma and inflammation)

IT 477251-83-5P, N-Isopropyl-1-[3-(4-acetylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-87-9P, N-Isopropyl-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-91-5P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-92-6P, N-Isopropyl-1-[3-[4-[4-(tert-butyloxycarbonyl)piperazin-1-yl]phenyl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-93-7P, N-Isopropyl-1-[3-(quinolin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-95-9P, N-Cyclopropyl-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-97-1P, N-Isopropyl-1-[3-(5-methylthiopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-99-3P, N-Cyclopropyl-1-[3-(4-hydroxymethylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-00-9P, N-Cyclopropyl-1-[3-(pyridin-4-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-01-0P, N-Cyclopropyl-1-[3-(4-ethylthiophenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-05-4P, N-Isopropyl-1-[3-(4-methylthiophenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-07-6P, N-Isopropyl-1-[3-(5-carboethoxypyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-08-7P, N-Isopropyl-1-[3-[5-(1-hydroxy-1-methylethyl)pyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-09-8P, N-Isopropyl-1-[3-[6-(2-methylpropyl)pyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-11-2P, N-Isopropyl-1-[3-(6-methylpyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-23-6P, N-Cyclopropyl-1-[3-(6-methylpyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-25-8P, N-Cyclopropyl-1-[3-(5-bromopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-26-9P, N-Cyclopropyl-1-[3-(6-benzyloxypyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-31-6P, N-Isobutyl-1-[3-[6-(1-hydroxy-1-methylethyl)pyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-32-7P, N-Cyclopropyl-1-[5-bromo-3-[6-(1-hydroxy-1-methylethyl)pyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-35-0P, N-Cyclopropyl-1-[3-(6-methylsulfonylpyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-43-0P, N-Cyclopropyl-1-[3-[5-[6-(1-hydroxy-1-methylethyl)pyridin-3-yl]pyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide
RL: **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(PDE4 inhibitor; preparation of biarylnaphthyridinone PDE4 inhibitors by

cyclization and arylation of (arylamino)(nicotinoyl)acrylates for treatment of asthma and inflammation)

IT 477251-76-6P, N-Isopropyl-1-[3-(3-acetylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-80-2P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(3-acetylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-82-4P, N-Isopropyl-1-[3-(4-n-propylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-84-6P, N-Isopropyl-1-[3-(2-methylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-85-7P, N-Isopropyl-N-methyl-1-[3-(4-acetylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-88-0P, N-Isopropyl-1-[3-(indol-5-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-89-1P, N-tert-Butyl-1-[3-(4-acetylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-94-8P, N-Isopropyl-1-[3-(pyrimidin-5-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-02-1P, N-Cyclopropyl-1-[3-(3-thienyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-03-2P, N-Cyclopropyl-1-[3-(4-sulfamoylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-04-3P, N-Isopropyl-1-[3-(3-ethoxyphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-06-5P, N-Isopropyl-1-[3-(3-acetyl-4-hydroxyphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-10-1P, N-Isopropyl-1-[3-(5-acetylpyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-12-3P, N-Cyclopropyl-1-[3-(1-oxidopyrimidin-5-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-13-4P, 1-[3-[6-(1-Hydroxy-1-methylethyl)-1-oxidopyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-14-5P, N-Isopropyl-1-[3-[4-(pyridin-3-yl)phenyl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-15-6P, N-Cyclopropyl-1-[3-(5-methylsulfonylpyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-16-7P, N-Cyclopropyl-1-[3-[4-(1-hydroxy-1-methylethyl)-1-oxidopyridin-2-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-17-8P, N-Cyclopropyl-1-[3-[5-(1-hydroxy-1-methylethyl)pyridin-2-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-18-9P, N-Cyclopropyl-1-[3-[3-(1-hydroxy-1-methylethyl)pyridin-4-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-19-0P, N-Cyclopropyl-1-[3-[3-(1-hydroxy-1-methylethyl)-1-oxidopyridin-4-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-21-4P, N-Cyclopropyl-1-[3-(6-isopropylsulfonylpyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-22-5P, N-Cyclopropyl-1-[3-(6-methoxypyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-24-7P, N-Cyclopropyl-1-[3-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-27-0P, N-Cyclopropyl-1-[3-[6-dicyclopropyl(hydroxy)methyl-1-oxidopyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-28-1P, N-Cyclopropyl-1-[3-[5-(1-hydroxy-1-methylethyl)-1-oxidopyridin-2-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-30-5P, N-Cyclopropyl-1-[3-[6-(1-hydroxy-1-methylethyl)pyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-33-8P, N-Cyclopropyl-1-[3-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-34-9P, N-Isopropyl-1-[3-(4-methylsulfonylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-36-1P, N-Isopropyl-1-[3-(5-methylsulfonylpyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-37-2P, N-Cyclopropyl-1-[3-(4-ethylsulfonylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-38-3P, N-Cyclopropyl-1-[3-(4-ethylsulfinylphenyl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-39-4P,

N-Isopropyl-1-[3-[4-(1-oximidoethyl)phenyl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-40-7P, N-Isopropyl-1-[3-[4-(piperazin-1-yl)phenyl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-41-8P, N-Cyclopropyl-1-[3-[4-(methylsulfonylmethyl)phenyl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-42-9P, N-Cyclopropyl-1-[3-(1,6-dihydro-6-oxopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-44-1P, N-Isopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-45-2P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-46-3P, N-Isopropyl-1-[3-(5-carboethoxy-1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-47-4P, N-Isopropyl-1-[3-[5-(1-hydroxy-1-methylethyl)-1-oxidopyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-48-5P, N-Isopropyl-1-[3-[6-(2-methylpropyl)-1-oxidopyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-49-6P, N-Isopropyl-1-[3-(6-methyl-1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-50-9P, N-Cyclopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-51-0P, N-Cyclopropyl-1-[3-[6-(1-hydroxy-1-methylethyl)-1-oxidopyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-53-2P, N-Cyclopropyl-1-[3-(1-oxidopyridin-4-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-54-3P, N-Cyclopropyl-1-[3-(5-bromo-1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-55-4P, N-Cyclopropyl-1-[[3-[5-[6-(1-hydroxy-1-methylethyl)-1-oxidopyridin-3-yl]pyridin-3-yl]phenyl]]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-56-5P, N-Cyclopropyl-1-[[3-[5-[6-(1-hydroxy-1-methylethyl)pyridin-3-yl]-1-oxidopyridin-3-yl]phenyl]]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-57-6P, N-Cyclopropyl-1-[[3-[5-[6-(1-hydroxy-1-methylethyl)-1-oxidopyridin-3-yl]-1-oxidopyridin-3-yl]phenyl]]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-58-7P, N-Isopropyl-1-[3-(1-oxidoquinolin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-59-8P, N-Isobutyl-1-[3-[6-(1-hydroxy-1-methylethyl)-1-oxidopyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-60-1P, N-Cyclopropyl-1-[3-(6-methyl-1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-61-2P, N-Cyclopropyl-1-[3-(6-methylsulfonyl-1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-62-3P, N-Cyclopropyl-1-[5-bromo-3-[6-(1-hydroxy-1-methylethyl)-1-oxidopyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-63-4P, N-Cyclopropyl-1-[3-[6-(1,2-dihydroxy-1-methylethyl)-1-oxidopyridin-3-yl]phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-64-5P 477252-65-6P

RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4 inhibitor; preparation of biarylnaphthyridinone PDE4 inhibitors by cyclization and arylation of (arylamino)(nicotinoyl)acrylates for treatment of asthma and inflammation)

IT 60-92-4, CAMP 61-19-8, AMP, biological studies **9036-21-9**, Phosphodiesterase IV

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation of biarylnaphthyridinone PDE4 inhibitors by cyclization and arylation of (arylamino)(nicotinoyl)acrylates for treatment of asthma and inflammation)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 22 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:716093 HCAPLUS Full-text
DOCUMENT NUMBER: 137:226611
TITLE: Use of **type 4 phosphodiesterase** inhibitors in myocardial diseases
INVENTOR(S): Sutter, Arne; Ehring, Thomas; Welge, Thomas; Minck, Klaus; Wilm, Claudia; Gassen, Michael; Eggenweiler, Hans-Michael; Wolf, Michael; Schelling, Pierre; Beier, Norbert; Leibrock, Joachim
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002072103	A1	20020919	WO 2002-EP320		20020115 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2437932	A1	20020919	CA 2002-2437932		20020115 <--
AU 2002228047	A1	20020924	AU 2002-228047		20020115 <--
EP 1368035	A1	20031210	EP 2002-710008		20020115 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 200303181	A2	20040128	HU 2003-3181		20020115 <--
CN 1491112	A	20040421	CN 2002-804877		20020115 <--
JP 2004521928	T	20040722	JP 2002-571062		20020115 <--
NO 2003003541	A	20030811	NO 2003-3541		20030811 <--
US 2005070529	A1	20050331	US 2004-467793		20041123 <--
PRIORITY APPLN. INFO.:			EP 2001-102811	A	20010212 <--
			EP 2001-119875	A	20010817 <--
			WO 2002-EP320	W	20020115 <--

OTHER SOURCE(S): MARPAT 137:226611
ED Entered STN: 20 Sep 2002
AB The invention relates to the use of type 4 phosphodiesterase inhibitors to treat myocardial diseases.
IC ICM A61K031-54
ICS A61K031-535; A61K031-50; A61P009-00
CC **1-8** (Pharmacology)
IT Cell proliferation
(T cell; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Ischemia
(cardiac; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Heart, disease
(failure; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)

IT Heart, disease
(infarction; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Reperfusion
(injury; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Heart, disease
(ischemia; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Human
(monocytes; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT T cell (lymphocyte)
(proliferation; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Injury
(reperfusion; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT **Artery, disease**
(**restenosis**; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Anti-ischemic agents
(use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Interleukin 10
Interleukin 12
Interleukin 2
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT **9036-21-9**, Phosphodiesterase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)
IT 61413-54-5, Rolipram 180600-64-0 180600-67-3 183582-59-4
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94360 188983-99-5 188984-02-3 188984-03-4 188984-04-5
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203382-46-1 203382-49-4 252724-14-4, EMD 219901 265996-73-4
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299896-13-2 299896-14-3 299896-15-4 299896-16-5 299896-17-6
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RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of **type 4 phosphodiesterase** inhibitors in myocardial diseases)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 23 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:695783 HCAPLUS Full-text
DOCUMENT NUMBER: 137:216886
TITLE: Preparation of 8-(alkenylaryl)quinoline **phosphodiesterase-4** inhibitors
INVENTOR(S): Vailaya, Anant; Conlon, David A.; Ho, Guo-Jie; Macdonald, Dwight; Perrier, Helene; Thibert, Roch; Kwong, Elizabeth; Clas, Sophie-Dorothee
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Merck Frosst Canada & Co.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069970	A1	20020912	WO 2001-US48674	20011214 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002143032	A1	20021003	US 2001-40993	20011109 <--
US 6740666	B2	20040525		
CA 2431549	A1	20020912	CA 2001-2431549	20011214 <--
AU 2001297603	A1	20020919	AU 2001-297603	20011214 <--
EE 200300266	A	20031015	EE 2003-266	20011214 <--
EP 1363635	A1	20031126	EP 2001-273908	20011214 <--
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BR 2001016372	A	20031209	BR 2001-16372		20011214	<--
HU 200400654	A2	20040628	HU 2004-654		20011214	<--
JP 2004521921	T	20040722	JP 2002-569145		20011214	<--
CN 1551769	A	20041201	CN 2001-822760		20011214	<--
NZ 526376	A	20050225	NZ 2001-526376		20011214	<--
BG 107900	A	20040630	BG 2003-107900		20030611	<--
ZA 2003004672	A	20040421	ZA 2003-4672		20030617	<--
NO 2003002807	A	20030815	NO 2003-2807		20030619	<--
IN 2003CN01089	A	20050422	IN 2003-CN1089		20030717	<--
PRIORITY APPLN. INFO.:			US 2000-256803P	P	20001220	<--
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OTHER SOURCE(S): MARPAT 137:216886
ED Entered STN: 13 Sep 2002
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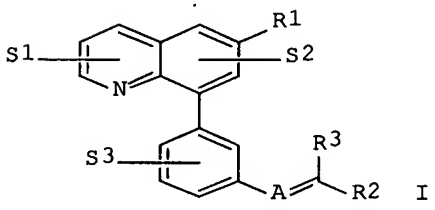

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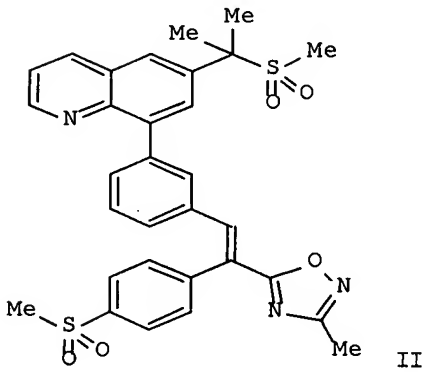


II

AB Title compds. I [wherein S1-S3 = independently H, OH, halo, NO2, CN, or (un)substituted alkyl or alkoxy; R1 = H, OH, halo, or (un)substituted acyl, (cyclo)alkyl, alkenyl, alkoxy, (hetero)aryl, heterocycloalkyl, NH2, carbamoyl, sulfamoyl , etc.; A = CH, C-ester, or CR4; R2 and R3 = independently H, halo, CN, CO2H, or (un)substituted (hetero)aryl, (heterocyclo)alkyl, alkoxy, acyl, carbamoyl, etc.; with the proviso that 1 of R2 and R3 must = (hetero)aryl; when R2 and R2 both = (hetero)aryl, then R2 and R3 may be optionally connected by a thio, oxy, or alkyl bridge to from a fused 3-ring system; R4 = CN or (un)substituted (hetero)aryl, alkyl, acyl, carbamoyl, etc.; or R2 or R3 may be optionally joined to R4 by a bond to form a ring; n = 0-2; and pharmaceutically acceptable H2SO4, methanesulfonic acid, p-toluenesulfonic acid, 2-naphthalenesulfonic acid, hydrochloride acid, or benzenesulfonic acid salts thereof] were prepared as phosphodiesterase-4 (PDE4) inhibitors. For example, a solution of (E)-1-(3-bromophenyl)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4- (methylsulfonyl)phenyl]ethene, diboron pinacol ester, [1,1'-bis(diphenylphosphino)ferrocene]PdCl2, and KOAc in DMF was stirred at 80° for 3 h. Sequential addition of 6-[1-methyl-1- (methylsulfonyl)ethyl]-8-bromoquinoline, [1,1'- bis(diphenylphosphino)ferrocene]PdCl2, and Na2CO3 followed by heating at 80° overnight gave (E)- and (Z)-II. Forty-two compds. of the invention exhibited IC50 values ranging from 0.04 μM to 8.71 μM in LPS and fMLP-induced TNF-α and LTB4 assays performed on human whole blood. All but one of same compds. inhibited the hydrolysis of cAMP to AMP by type-IV cAMP-specific phosphodiesterases with IC50 values ranging from 0.14 nM to 10.24 nM. Thus, I are useful as anti-inflammatory and anti-allergic agents

for treatment of a wide variety of PDE4-related diseases and conditions (no data).

IC ICM A61K031-47
ICS C07D215-12; C07D215-14; C07D401-10; C07D413-10; C07D417-10; A61P011-00

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT Inflammation
(Crohn's disease; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Intestine, disease
(Crohn's; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Antihistamines
(H1, combination therapy agent; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Muscarinic antagonists
(M2, combination therapy agent; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Muscarinic antagonists
(M3, combination therapy agent; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Respiratory distress syndrome
(adult; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Allergy
Inflammation
Nose, disease
(allergic rhinitis; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Inflammation
Spinal column, disease
(ankylosing spondylitis; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Dermatitis
(atopic; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Skin, disease
(benign or malignant proliferative; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Bronchi, disease
Inflammation
(chronic bronchitis; preparation of (alkenylaryl)quinoline

phosphodiesterase-4 inhibitors with anti-inflammatory and anti-allergic activity)

IT Lung, disease
(chronic obstructive pulmonary disease; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Leukotriene antagonists
β2-Adrenoceptor agonists
(combination therapy agent; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Corticosteroids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination therapy agent; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Nervous system, disease
(degeneration; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Mental and behavioral disorders
(depression; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Granulomatous disease
(eosinophilic; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Inflammation
Kidney, disease
(glomerulonephritis, chronic; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Transplant and Transplantation
(graft-vs.-host reaction; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Injury
(head and neck; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Gastric acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hypersecretion; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Memory, biological
(impairment; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Reperfusion
(injury, myocardial or brain; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Head and Neck, disease
(injury; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Anti-inflammatory agents
(neurogenic and non-neurogenic; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory

and anti-allergic activity)

IT Inflammation
(neurogenic; preparation of (alkenylaryl)quinoline **phosphodiesterase -4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Respiratory distress syndrome
(newborn; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Anti-inflammatory agents
(nonsteroidal, combination therapy agent; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Antiarthritics
Antiasthmatics
Antibacterial agents
Antidepressants
Antirheumatic agents
Antitumor agents
Antitussives
Antiviral agents
Asthma
Atherosclerosis
Cognition enhancers
Cough
Diabetes insipidus
Fungicides
Human
Inflammation
Multiple sclerosis
Neoplasm
Osteoporosis
Pain
Psoriasis
Rheumatoid arthritis
Sepsis
Transplant rejection
Urticaria
(preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Brain
Heart
(reperfusion injury; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Injury
(reperfusion, myocardial or brain; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT **Artery, disease**
(**restenosis**; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Shock (circulatory collapse)

(septic; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Proteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(statin, combination therapy agent; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Multiple sclerosis
Osteoporosis
(therapeutic agents; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Spinal cord, disease
(trauma; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT Inflammation
Intestine, disease
(ulcerative colitis; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT 329900-75-6, COX 2
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(COX-2 selective inhibitor, combination therapy agent; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT 346629-30-9P, 6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-[3-[(E)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-34-3P, 8-[3-[(E)-2-[3-[(4-Methoxyphenoxy)methyl]-1,2,4-oxadiazol-5-yl]-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]-6-[1-methyl-1-(methylsulfonyl)ethyl]quinoline
RL: **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(PDE4 inhibitor; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT 346629-17-2P, 6-Isopropyl-8-[3-[(Z)-2-[4-(methylsulfonyl)phenyl]-2-phenylethenyl]phenyl]quinoline 346629-18-3P, 6-Isopropyl-8-[3-[(E)-2-[4-(methylsulfonyl)phenyl]-2-phenylethenyl]phenyl]quinoline 346629-19-4P, 6-Isopropyl-8-[3-[2-[4-(methylsulfonyl)phenyl]-2-(1,3-thiazol-2-yl)ethenyl]phenyl]quinoline 346629-20-7P, 6-Isopropyl-8-[3-[(E)-2-(1-methyl-1H-imidazol-2-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-21-8P, 6-Isopropyl-8-[3-[(Z)-2-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-22-9P, 6-Isopropyl-8-[3-[(E)-2-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-23-0P, 2-[2-[2-[3-(6-Isopropyl-8-quinolinyl)phenyl]-1-[4-(methylsulfonyl)phenyl]ethenyl]-1,3-thiazol-5-yl]-2-propanol 346629-24-1P, 2-[8-[3-[2-[5-(1-Hydroxy-1-methylethyl)-1,3-thiazol-2-yl]-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]-6-quinolinyl]-2-methylpropanenitrile 346629-25-2P, 2-Methyl-2-[8-[3-[(E)-2-(1-methyl-1H-imidazol-2-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]-6-quinolinyl]propanenitrile 346629-26-3P, 6-[1-(Methylsulfonyl)ethyl]-8-[3-[(E)-2-[4-(methylsulfonyl)phenyl]-2-(1,3-thiazol-2-yl)ethenyl]phenyl]quinoline 346629-27-4P, 6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-[3-[(E)-2-[4-(methylsulfonyl)phenyl]-2-(1,3-thiazol-2-yl)ethenyl]phenyl]quinoline 346629-28-5P, 8-[3-[(Z)-2-(1-Methyl-1H-imidazol-2-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]-6-[1-(methylsulfonyl)ethyl]quinoline 346629-29-6P, 8-[3-[(Z)-2-(1-Methyl-1H-imidazol-2-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]-6-[1-methyl-1-

(methylsulfonyl)ethyl]quinoline 346629-31-0P, 6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-[3-[(Z)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-32-1P, (E)-3-[3-[6-(1-Cyano-1-methylethyl)-8-quinolinyl]phenyl]-N-isopropyl-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-35-4P, [5-[(E)-2-[3-[6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl]phenyl]-1-[4-(methylsulfonyl)phenyl]ethenyl]-1,2,4-oxadiazol-3-yl]methanol 346629-36-5P, (E)-N-Isopropyl-3-[3-[6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl]phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-39-8P, 2-Methyl-2-[8-[3-[(E)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]-6-quinolinyl]propanenitrile 346629-40-1P, (E)-3-[3-[6-(1-Cyano-1-methylethyl)-8-quinolinyl]phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-41-2P, (E)-N-(tert-Butyl)-3-[3-[6-(1-cyano-1-methylethyl)-8-quinolinyl]phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-42-3P, (E)-3-[3-(6-Isopropyl-8-quinolinyl)phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenoic acid 346629-43-4P, 6-Isopropyl-8-[3-[(E)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-44-5P, (E)-3-[3-[6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl]phenyl]-2-[4-(methylsulfonyl)phenyl]-1-(1-pyrrolidinyl)-2-propen-1-one 346629-45-6P, (E)-N-Cyclopropyl-3-[3-[6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl]phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-46-7P, (E)-N-(tert-Butyl)-3-[3-[6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl]phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-47-8P, 8-[3-[2,2-Bis(4-chlorophenyl)vinyl]phenyl]-6-isopropylquinoline 346629-48-9P, 6-Isopropyl-8-[3-[(E)-2-(6-methyl-3-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-49-0P, 6-Isopropyl-8-[3-[(Z)-2-(6-methyl-3-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-50-3P, 6-Isopropyl-8-[3-[(E)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-51-4P, 6-Isopropyl-8-[3-[(Z)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-52-5P, 8-[3-[2,2-Bis[4-(methylsulfonyl)phenyl]vinyl]phenyl]-6-isopropylquinoline 346629-53-6P, 2-Methyl-2-[8-[3-[(E)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]-6-quinolinyl]propanenitrile 346629-54-7P, 2-Methyl-2-[8-[3-[(Z)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]-6-quinolinyl]propanenitrile 346629-57-0P, 6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-[3-[(E)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-58-1P, 6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-[3-[(Z)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl]phenyl]quinoline 346629-59-2P, 2-[6-[(E)-2-[3-[6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl]phenyl]-1-[4-(methylsulfonyl)phenyl]ethenyl]-3-pyridinyl]-2-propanol 346630-04-4P 346630-05-5P 346630-06-6P 346630-07-7P 455948-57-9P, (E)-3-[3-[6-(1-Cyano-1-methylethyl)-8-quinolinyl]phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenoic acid 455948-59-1P, 2-[8-[3-[2,2-Bis[4-(methylsulfonyl)phenyl]vinyl]phenyl]-6-quinolinyl]-2-methylpropanenitrile 455948-60-4P, 2-Methyl-2-[8-[3-[(E)-2-[4-(methylsulfonyl)phenyl]-2-(2-pyridinyl)ethenyl]phenyl]-6-quinolinyl]propanenitrile

RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4 inhibitor; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT 724-88-9P, (4-Fluorophenyl) [4-(methylthio)phenyl] ketone 346629-38-7P, (E)-3-[3-[6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl]phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenoic acid 346629-79-6P 346629-80-9P,

2-(3-Bromophenyl)-1-(1,3-thiazol-2-yl)-1-[4-(methylthio)phenyl]ethene 346629-81-0P, 2-(3-Bromophenyl)-1-(1,3-thiazol-2-yl)-1-[4-(methylsulfonyl)phenyl]ethene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT 346630-09-9P
RL: **PAC (Pharmacological activity)**; PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymorph Form A and Form B, PDE4 inhibitor; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT 60-92-4, CAMP 61-19-8, AMP, biological studies **9036-21-9** 71160-24-2, Leukotriene B4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT 346629-60-5DP, salts
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

IT 75-64-9, tert-Butylamine, reactions 90-98-2, 4,4'-Dichlorobenzophenone 123-75-1, Pyrrolidine, reactions 150-76-5, 4-Methoxyphenol 352-13-6, 4-Fluorophenylmagnesium bromide 765-30-0, Cyclopropylamine 3132-99-8, 3-Bromobenzaldehyde 3446-89-7, 4-(Methylthio)benzaldehyde 21205-06-1 87199-16-4, 3-Formylbenzeneboronic acid 90536-66-6, 4-(Methylsulfonyl)phenylacetic acid 95898-78-5, (2-Pyridinyl)[4-(methylsulfonyl)phenyl] ketone 95902-10-6, (3-Bromobenzyl)(triphenyl)phosphonium bromide 197438-91-8, (4-Fluorophenyl)[4-(methylsulfonyl)phenyl] ketone 346629-61-6, (1-Methyl-1H-imidazol-2-yl) [4-(methylthio)phenyl] ketone 346629-65-0, (1,3-Thiazol-2-yl) [4-(methylsulfonyl)phenyl] ketone 346629-66-1, [5-(1-Hydroxy-1-methylethyl)-1,3-thiazol-2-yl] [4-(methylsulfonyl)phenyl] ketone 346629-68-3, (6-Methyl-3-pyridinyl) [4-(methylsulfonyl)phenyl] ketone 346629-71-8, (5-Methyl-2-pyridinyl)[4-(methylsulfonyl)phenyl] ketone 346629-72-9, Bis[(4-methylsulfonyl)phenyl] ketone 346629-76-3 346629-82-1, (E)-3-(3-Bromophenyl)-2-[4-(methylsulfonyl)phenyl]-2-propenoic acid 346629-83-2, (E)-1-(3-Bromophenyl)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethene 346629-85-4, [3-(6-Isopropyl-8-quinolinyl)benzyl](triphenyl)phosphonium Bromide 346629-88-7 346629-89-8 346629-92-3 346629-94-5, (E)-N-Isopropyl-3-(3-bromophenyl)-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-95-6, (E)-3-(3-Bromophenyl)-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-96-7, (E)-N-(tert-Butyl)-3-(3-Bromophenyl)-2-[4-(methylsulfonyl)phenyl]-2-propenamide 346629-98-9, 6-[1-(Methylsulfonyl)ethyl]-8-bromoquinoline 346629-99-0, 6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-bromoquinoline 346630-01-1, 6-(1-Methyl-1-cyanoethyl)-8-bromoquinoline 346630-03-3, 3-[6-[1-Methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl]benzaldehyde 455948-56-8 455948-58-0, 5-Isopropyl-8-bromoquinoline
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of (alkenylaryl)quinoline **phosphodiesterase-4** inhibitors with anti-inflammatory and anti-allergic activity)

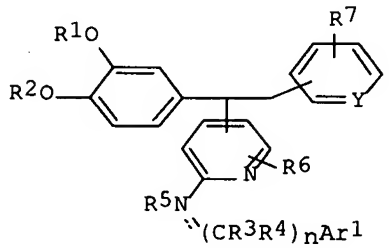
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L76 ANSWER 24 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:814461 HCAPLUS Full-text
DOCUMENT NUMBER: 133:362707
TITLE: Preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors.
INVENTOR(S): Cote, Bernard; Friesen, Richard; Frenette, Richard; Girard, Mario; Girard, Yves; Godbout, Cedrickx; Guay, Daniel; Hamel, Pierre; Blouin, Marc; Ducharme, Yves; Prescott, Sylvie
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068198	A2	20001116	WO 2000-CA500	20000503 <--
WO 2000068198	A3	20010405		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6200993	B1	20010313	US 2000-551040	20000417 <--
CA 2369323	A1	20001116	CA 2000-2369323	20000503 <--
EP 1177175	A2	20020206	EP 2000-922400	20000503 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 764258	B2	20030814	AU 2000-42829	20000503 <--
PRIORITY APPLN. INFO.:			US 1999-132532P P	19990505 <--
			WO 2000-CA500 W	20000503 <--

OTHER SOURCE(S): MARPAT 133:362707
ED Entered STN: 21 Nov 2000
GI



I

AB Title compds. [I; Y = N, NO; R1, R2 = H, alkyl, haloalkyl; R3, R4 = H, alkyl; R3R4 = O, atoms to form a 5-7 membered carbocyclic ring; R5 = null, H,

(substituted) alkyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, O; R3R5 = atoms to form a 5-6 membered heterocyclic ring; dotted line = optional double bond; R6, R7 = H, halo, alkyl, haloalkyl, cyano; n = 0-6], were prepared Thus, 4-[2-[3,4-bis(difluoromethoxy)phenyl]- 2-(6-bromo-3-pyridyl)ethyl]pyridine (preparation given) was heated with PhCH2NH2 and CuI to give 72% 4-[2-[3,4-bis(difluoromethoxy)phenyl]-2-[6- (benzylamino)-3-pyridyl]ethyl]pyridine. The latter inhibited PDE 4 with IC50 = 0.75 nM.

IC ICM C07D213-89
ICS C07D213-74; C07D417-14; C07D401-14; C07D409-14; C07D213-79; C07D213-76; C07D405-14; A61K031-4427; A61P011-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT Intestine, disease
(Crohn's, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Respiratory distress syndrome
(adult, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Eye, disease
(allergic conjunctivitis, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Nose
(allergic rhinitis, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Spinal column
(ankylosing spondylitis, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Dermatitis
(atopic, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Bronchi
(chronic bronchitis, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Granuloma
(eosinophilic, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Kidney, disease
(glomerulonephritis, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Lung, disease
Respiratory tract
(inflammation, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Cachexia
(inhibitors; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Reperfusion
(injury, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Inflammation
(neurogenic, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Analgesics
Antiarthritics
Antiasthmatics
Antidepressants
Antitumor agents
Antitussives
(preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Skin, disease
(proliferative, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT **Artery, disease**
(**restenosis**, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Gastric acid
(secretion, inhibitors; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Shock (circulatory collapse)
(septic, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Spinal column
(spondylitis, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Animal tissue
(treatment of tissue degeneration; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Cystic fibrosis
Diabetes insipidus
Psoriasis
Sepsis
Transplant rejection
Urticaria
(treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Intestine, disease
(ulcerative colitis, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT Muscle, disease
(wasting, treatment; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT **9036-21-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(IV, inhibitors; preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT 306760-71-4P 306760-72-5P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT 306760-69-0P 306760-86-1P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT 306759-92-2P 306759-93-3P 306759-94-4P 306759-95-5P 306759-96-6P
306759-97-7P 306759-98-8P 306759-99-9P 306760-00-9P 306760-01-0P
306760-02-1P 306760-03-2P 306760-04-3P 306760-05-4P 306760-06-5P
306760-07-6P 306760-08-7P 306760-09-8P 306760-10-1P 306760-11-2P
306760-12-3P 306760-13-4P 306760-14-5P 306760-15-6P 306760-16-7P
306760-17-8P 306760-18-9P 306760-19-0P 306760-20-3P 306760-21-4P
306760-22-5P 306760-23-6P 306760-24-7P 306760-25-8P 306760-26-9P
306760-27-0P 306760-28-1P 306760-29-2P 306760-30-5P 306760-31-6P
306760-32-7P 306760-33-8P 306760-34-9P 306760-35-0P 306760-36-1P
306760-37-2P 306760-38-3P 306760-39-4P 306760-40-7P 306760-41-8P
306760-42-9P 306760-43-0P 306760-44-1P 306760-45-2P 306760-46-3P
306760-47-4P 306760-48-5P 306760-49-6P 306760-50-9P 306760-51-0P
306760-52-1P 306760-53-2P 306760-54-3P 306760-55-4P 306760-56-5P
306760-57-6P 306760-58-7P 306760-59-8P 306760-60-1P 306760-61-2P
306760-62-3P 306760-63-4P 306760-64-5P 306760-65-6P 306760-66-7P
306760-67-8P 306760-68-9P 306760-70-3P 306760-73-6P 306760-74-7P
306760-75-8P 306760-76-9P 306760-77-0P 306760-78-1P 306760-79-2P
306760-80-5P 306760-81-6P 306760-82-7P 306760-83-8P 306760-84-9P
306760-85-0P 306760-87-2P 306760-88-3P 306760-90-7P 306760-91-8P
306760-92-9P 306760-93-0P 306760-94-1P 306760-95-2P 306760-96-3P
306771-52-8P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT 64-04-0, Phenethylamine 75-16-1, Methylmagnesium bromide 91-21-4, 1,2,3,4-Tetrahydroisoquinoline 100-07-2, 4-Methoxybenzoyl chloride 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 100-61-8, N-Methylaniline, reactions 102-97-6, N-Isopropylbenzylamine 103-49-1, Dibenzylamine 103-67-3, N-Methylbenzylamine 104-11-0, N-Methyl-4-chlorobenzylamine 104-63-2, N-Benzylethanolamine 140-75-0, 4-Fluorobenzylamine 403-40-7, 1-(4-Fluorophenyl)ethylamine 403-43-0, 4-Fluorobenzoyl chloride 459-22-3, 4-Fluorophenylacetonitrile 585-32-0, Cumylamine 589-08-2, N-Methylphenethylamine 624-28-2, 2,5-Dibromopyridine 658-93-5, 3,4-Difluorophenylacetic acid 767-00-0, 4-Cyanophenol 874-33-9 917-54-4, Methyllithium 1006-64-0, 2-Phenylpyrrolidine 1194-02-1, 4-Fluorobenzonitrile 1200-27-7 1583-88-6, 2-(4-Fluorophenyl)ethylamine 2627-86-3, (S)-1-Phenylethylamine 2706-56-1, 2-(2-Aminoethyl)pyridine 2975-41-9, 2-Aminoindane 3082-64-2, (R)-1-Phenylpropylamine 3378-72-1, N-tert-Butylbenzylamine 3731-51-9, 2-Aminomethylpyridine 3886-69-9, (R)-1-Phenylethylamine 5933-40-4 5961-59-1, N-Methyl-4-methoxyaniline 6526-79-0 10277-74-4 14321-27-8, N-Ethylbenzylamine 17797-11-4 19131-99-8 20173-04-0 30568-40-2 34698-41-4, 1-Aminoindane 41789-95-1, N-Methyl-3-methoxybenzylamine 52568-28-2 54401-85-3, Ethyl 4-pyridylacetate 61341-86-4 72235-52-0, 2,4-Difluorobenzylamine 74702-89-9 74702-93-5 76532-33-7 127842-54-0, 3,4-Bis(difluoromethoxy)benzaldehyde 130416-51-2 160001-92-3 194736-72-6 306761-54-6 306761-55-7 306761-56-8 306761-57-9 306761-58-0 306761-59-1 306761-60-4 306761-61-5 306761-62-6 306771-54-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

IT 17797-10-3P 40377-35-3P 52805-36-4P 90446-25-6P, 4-Difluoromethoxybenzonitrile 93748-09-5P 210530-71-5P 303165-20-0P 303165-21-1P 303165-22-2P 303165-23-3P 306760-97-4P 306760-98-5P 306760-99-6P 306761-00-2P 306761-01-3P 306761-02-4P 306761-03-5P 306761-04-6P 306761-05-7P 306761-06-8P 306761-07-9P 306761-08-0P

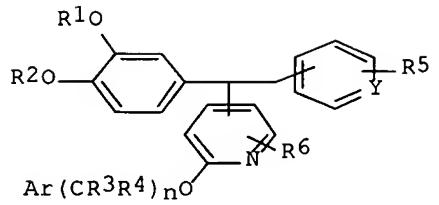
306761-09-1P 306761-10-4P 306761-11-5P 306761-12-6P 306761-13-7P
306761-14-8P 306761-15-9P 306761-16-0P, Methyl 2-methyl-2-(3,4-
difluorophenyl)propionate 306761-17-1P 306761-18-2P 306761-19-3P
306761-20-6P 306761-21-7P 306761-22-8P 306761-23-9P 306761-24-0P
306761-25-1P 306761-26-2P 306761-27-3P 306761-28-4P 306761-29-5P
306761-30-8P 306761-31-9P 306761-32-0P 306761-33-1P 306761-34-2P
306761-35-3P 306761-36-4P 306761-37-5P 306761-38-6P 306761-39-7P
306761-40-0P 306761-41-1P 306762-42-2P 306761-43-3P 306761-44-4P
306761-45-5P 306761-46-6P 306761-47-7P 306761-48-8P 306761-49-9P
306761-50-2P 306761-51-3P 306761-52-4P 306761-53-5P 306761-63-7P
306762-34-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridylethylpyridines as **phosphodiesterase 4** inhibitors)

L76 ANSWER 25 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:772611 HCAPLUS Full-text
DOCUMENT NUMBER: 133:335161
TITLE: Preparation of pyridylethylpyridines and related compounds as phosphodiesterase IV inhibitors.
INVENTOR(S): Frenette, Richard; Friesen, Richard; Girard, Mario; Girard, Yves; Godbout, Cedrickx; Guay, Daniel; Hamel, Pierre; Perrier, Helene
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064874	A2	20001102	WO 2000-CA427	20000419 <--
WO 2000064874	A3	20010215		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6180650	B1	20010130	US 2000-525600	20000314 <--
CA 2369092	A1	20001102	CA 2000-2369092	20000419 <--
EP 1180100	A2	20020220	EP 2000-918641	20000419 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-130690P P 19990423 <--
WO 2000-CA427 W 20000419 <--

OTHER SOURCE(S): MARPAT 133:335161
ED Entered STN: 03 Nov 2000
GI



I

AB Title compds. [I; Y = N, NO; R1, R2 = H, alkyl, haloalkyl; R3, R4 = H, alkyl; R3R4C = O; R3 and R4 on different C atoms = atoms to form a saturated 5-7 membered carbocyclic ring; R5, R6 = H, alkyl, haloalkyl, cyano; n = 0-6; Ar = (substituted) thienyl, thiazolyl, pyridyl, Ph, naphthyl], were prepared Thus, 4-[2-[3,4-bis(difluoromethoxy)phenyl]-2-[6-[4- (trifluoromethoxy)phenoxy]-3-pyridyl]ethyl]pyridine (preparation given) was stirred with monoperoxyphthalic acid in CH2Cl2 to give 97% 4-[2-[3,4-bis(difluoromethoxy)phenyl]-2-[6-[4-(trifluoromethoxy)phenoxy]-3- pyridyl]ethyl]pyridine N-oxide. The latter inhibited GST-Met 248 PDE4a with IC50 = 2.85 nM.

IC ICM C07D213-89
ICS C07D213-64; C07D409-14; C07D417-14; C07D213-79; C07D213-76; C07D405-14; A61K031-4427; A61P011-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28

IT Intestine, disease
(Crohn's, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Spinal column
(ankylosing spondylitis, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Dermatitis
(atopic, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Bronchi
(chronic bronchitis, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Eye, disease
(conjunctivitis, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Memory, biological
(disorder treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Kidney, disease
(glomerulonephritis, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Respiratory tract
(inflammation, treatment; preparation of pyridylethylpyridines and related

compds. as **phosphodiesterase 4** inhibitors)

IT Reperfusion
(injury, treatment; preparation of pyridylethylpyridines and related compds.
as **phosphodiesterase 4** inhibitors)

IT Analgesics
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidepressants
Antitumor agents
(preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT **Artery, disease**
(**restenosis**, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Gastric acid
(secretion, inhibitors; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Shock (circulatory collapse)
(septic, treatment; preparation of pyridylethylpyridines and related compds.
as **phosphodiesterase 4** inhibitors)

IT Animal tissue
(treatment of chronic tissue degeneration; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Cachexia
Cystic fibrosis
Granuloma
Psoriasis
Sepsis
Skin, disease
Transplant rejection
Urticaria
(treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Intestine, disease
(ulcerative colitis, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT Muscle, disease
(wasting, treatment; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT **9036-21-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(IV, inhibitors; preparation of pyridylethylpyridines and related compds. as
phosphodiesterase 4 inhibitors)

IT 60-92-4
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(increasing cAMP levels; preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT 303163-45-3P 303163-46-4P 303163-47-5P 303163-48-6P 303163-49-7P
303163-50-0P 303163-51-1P 303163-52-2P 303163-53-3P 303163-54-4P
303163-55-5P 303163-56-6P 303163-57-7P 303163-58-8P 303163-59-9P
303163-60-2P 303163-61-3P 303163-62-4P 303163-63-5P 303163-64-6P
303163-65-7P 303163-66-8P 303163-67-9P 303163-68-0P 303163-69-1P
303163-70-4P 303163-71-5P 303163-72-6P 303163-73-7P 303163-74-8P

303163-75-9P 303163-76-0P 303163-77-1P 303163-78-2P 303163-79-3P
303163-80-6P 303163-81-7P 303163-82-8P 303163-83-9P 303163-84-0P
303163-85-1P 303163-86-2P 303163-87-3P 303163-88-4P 303163-89-5P
303163-90-8P 303163-91-9P 303163-92-0P 303163-93-1P 303163-94-2P
303163-95-3P 303163-96-4P 303163-97-5P 303163-98-6P 303163-99-7P
303164-00-3P 303164-01-4P 303164-02-5P 303164-03-6P 303164-04-7P
303164-05-8P 303164-06-9P 303164-07-0P 303164-08-1P 303164-09-2P
303164-10-5P 303164-11-6P 303164-12-7P 303164-13-8P 303164-14-9P
303164-15-0P 303164-16-1P 303164-17-2P 303164-18-3P 303164-19-4P
303164-20-7P 303164-21-8P 303164-22-9P 303164-23-0P 303164-24-1P
303164-25-2P 303164-26-3P 303164-27-4P 303164-28-5P 303164-29-6P
303164-30-9P 303164-31-0P 303164-32-1P 303164-33-2P 303164-34-3P
303164-35-4P 303164-36-5P 303164-37-6P 303164-38-7P 303164-39-8P
303164-40-1P 303164-41-2P 303164-42-3P 303164-43-4P 303164-44-5P
303164-45-6P 303164-46-7P 303164-47-8P 303164-48-9P 303164-49-0P
303164-50-3P 303164-51-4P 303164-52-5P 303164-53-6P 303164-54-7P
303164-55-8P 303164-56-9P 303164-57-0P 303164-58-1P 303164-59-2P
303164-60-5P 303164-61-6P 303164-62-7P 303164-63-8P 303164-64-9P
303164-65-0P 303164-66-1P 303164-67-2P 303164-68-3P 303164-69-4P
303164-70-7P 303164-71-8P 303164-72-9P 303164-73-0P 303164-86-5P
303164-87-6P 303164-88-7P 303164-89-8P 303164-90-1P 303164-91-2P
303164-92-3P 303164-93-4P 303164-94-5P 303164-95-6P 303164-96-7P
303164-97-8P 303164-98-9P 303164-99-0P 303165-00-6P 303165-01-7P
303165-02-8P 303172-33-0P 303172-34-1P 303172-35-2P 303172-36-3P
303172-37-4P 303172-38-5P 303172-39-6P 303172-40-9P 303172-41-0P
303172-42-1P 303172-43-2P 303172-44-3P 303172-45-4P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT 75-16-1, Methylmagnesium bromide 98-85-1, 1-Phenylethanol 99-89-8, 4-Isopropylphenol 100-02-7, 4-Nitrophenol, reactions 100-51-6, Benzenemethanol, reactions 108-95-2, Phenol, reactions 349-95-1, 4-Trifluoromethylbenzyl alcohol 402-41-5 402-45-9, 4-Trifluoromethylphenol 459-56-3, 4-Fluorobenzyl alcohol 624-28-2, 2,5-Dibromopyridine 828-27-3, 4-Trifluoromethoxyphenol 873-76-7, 4-Chlorobenzyl alcohol 1736-74-9, 4-Trifluoromethoxybenzyl alcohol 3446-90-0, 4-Methylthiobenzyl alcohol 7589-27-7, 2-(4-Fluorophenyl)ethanol 34837-84-8, Methyl 4-fluorophenylacetate 55104-32-0, 6-Hydroxyphthalide 79538-20-8, 3,5-Difluorobenzyl alcohol 85118-05-4, 3,4-Difluorobenzyl alcohol 127842-54-0, 3,4-Bis(difluoromethoxy)benzaldehyde 303165-24-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

IT 703-10-6P 303165-03-9P 303165-04-0P 303165-05-1P 303165-06-2P
303165-07-3P 303165-08-4P 303165-09-5P 303165-10-8P 303165-11-9P
303165-12-0P 303165-13-1P 303165-14-2P 303165-15-3P 303165-16-4P
303165-17-5P 303165-18-6P 303165-19-7P 303165-20-0P 303165-21-1P
303165-22-2P 303165-23-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridylethylpyridines and related compds. as **phosphodiesterase 4** inhibitors)

L76 ANSWER 26 OF 57 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:15232 HCAPLUS Full-text
DOCUMENT NUMBER: 132:63147

TITLE: Monocyte locomotion **inhibitory** factor
INVENTOR(S): Schmid, Roberto Rodolfo Kretschmer
PATENT ASSIGNEE(S): The Center for Blood Research, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000511	A1	20000106	WO 1999-US14877	19990629 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
MX 9805265	A	20000831	MX 1998-5265	19980629 <--
CA 2331925	A1	20000106	CA 1999-2331925	19990629 <--
AU 9947291	A	20000117	AU 1999-47291	19990629 <--

PRIORITY APPLN. INFO.: MX 1998-5265 A 19980629 <--
WO 1999-US14877 W 19990629 <--

ED Entered STN: 07 Jan 2000

AB The invention relates to an anti-inflammatory oligopeptide which can be obtained from the microorganism Entamoeba histolytica or synthesized by known methods. The oligopeptides are useful in treating inflammatory diseases when formulated in pharmaceutical compns. for administration to patients.

IC ICM C07K014-44
CC 15-2 (Immunochemistry)
Section cross-reference(s): **1**, 3, 10, 63
ST Entamoeba histolytica monocyte locomotion **inhibitory** factor; antiinflammatory oligopeptide Entamoeba histolytica vaccine genetherapy
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1); Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
IT **Atherosclerosis**
Chemicals
Combinatorial library
Drugs
Entamoeba histolytica
Eye, disease
Gene therapy
Inflammation
Leukocyte
Lupus erythematosus
Macrophage
Molecular cloning
Neutrophil
Protein sequences
Psoriasis
Rheumatoid arthritis
Vaccines
(Entamoeba histolytica-derived monocyte locomotion **inhibitory**

factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Peptides, biological studies
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MLIF; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-κB (nuclear factor κB), activation; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Transplant rejection
(allotransplant; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT **Drug screening**
(anti-inflammatory; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Respiration, animal
(burst, **inhibition**; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Drug delivery systems
(carriers; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Nervous system
Periodontium
(disease; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Chemotaxis
(macrophage; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Microtiter plates
(multi-well; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Anti-inflammatory agents
(oligopeptide; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Peptides, biological studies
RL: PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(oligopeptides, antiinflammatory; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)

IT Peptide library
(random; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
IT Skin, disease
(scar, **inhibition**; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
IT Amebicides
(vaccine; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
IT 60-92-4, CAMP
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
IT 149370-57-0P, Monocyte motility-**inhibiting** factor
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
IT 253434-83-2 253434-86-5
RL: BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
IT **9036-21-9**, Phosphodiesterase IV
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**inhibitors**; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
IT 7727-37-9, Nitrogen, biological studies 7782-44-7, Oxygen, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(reactive; Entamoeba histolytica-derived monocyte locomotion **inhibitory** factor as antiinflammatory agent and anti-amoebic vaccine and recombinant vector for genetherapy)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l76 27-57 ibib ab ind

L76 ANSWER 27 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 1
ACCESSION NUMBER: 2000:448073 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000448073
TITLE: Studies on the vascular effects of the fractions and phenolic compounds isolated from Viscum album ssp. album.
AUTHOR(S): Deliorman, Didem [Reprint author]; Calis, Ihsan; Ergun, Fatma; Dogan, B. Sonmez Uydes; Buharalioglu, C. Kemal; Kanzik, Ilker

CORPORATE SOURCE: Faculty of Pharmacy, Gazi University, Hipodrom, Ankara, 06330, Turkey
SOURCE: Journal of Ethnopharmacology, (**September, 2000**) Vol. 72, No. 1-2, pp. 323-329. print.
CODEN: JOETD7. ISSN: 0378-8741.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 2000
Last Updated on STN: 10 Jan 2002

AB Viscum album L. has been used in the indigenous system of medicine for treatment of various diseases such as **atherosclerosis** and hypertension. In the literature, phenylpropan and flavonoid derivatives were suggested to play a role in the inhibition of cyclic adenosine monophosphate (cAMP)-phosphodiesterase (PDE) and a correlation was proposed between the in vitro inhibition of PDE and in vivo pharmacological activity. The vascular effects of the phenolic compounds and subfractions isolated from n-butanolic fraction of V. album ssp. album were studied on noradrenaline-contracted rat aortic rings. Isolated phenolic compounds (Syringin (VA-1), Coniferin (VA-9), 5,7-dimethoxy-flavanone-4'-O-(beta-D-apiofuranosyl(1 fwdarw 2))-beta-D-glucopyranoside (VA-4)) produced concentration-dependent contractions in rat aortic rings. Only one compound (Kalopanaxin D (VA-15)) displayed very slight relaxant response. The weak concentration-dependent relaxing effect of the subfractions gave the idea that vasodilator activity were observed in the less polar subfractions. In addition, there was no clear correlation between the weak relaxant effects of subfractions and an inhibitory effect on cAMP-PDE.

CC Allergy 35500
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Pharmacology - General 22002
Pharmacognosy and pharmaceutical botany 54000

IT Major Concepts
Pharmacology; Pharmacognosy (Pharmacology); Cardiovascular System (Transport and Circulation)

IT Parts, Structures, & Systems of Organisms
aortic rings: circulatory system

IT Diseases
atherosclerosis: vascular disease
Arteriosclerosis (MeSH)

IT Diseases
hypertension: vascular disease
Hypertension (MeSH)

IT Chemicals & Biochemicals
5,7-dimethoxy-flavanone-4'-O-[beta-D-apiofuranosyl(1-2)]-beta-D-glucopyranoside: phenolic compound; Coniferin: phenolic compound; Kalopanaxin D: phenolic compound; Syringin: phenolic compound; cyclic AMP-phosphodiesterase

ORGN Classifier
Loranthaceae 26305
Super Taxa
Dicotyledones; Angiospermae; Spermatophyta; Plantae
Organism Name
Viscum album album
Taxa Notes
Angiosperms, Dicots, Plants, Spermatophytes, Vascular Plants

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name

rat: male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN 531-29-3 (Coniferin)
136173-84-7 (Kalopanaxin D)
118-34-3 (Syringin)
9036-21-9 (cyclic AMP-phosphodiesterase)

L76 ANSWER 28 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:448522 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300448522
TITLE: Role of phosphodiesterase 3 in NO/cGMP-mediated antiinflammatory effects in vascular smooth muscle cells.
AUTHOR(S): Aizawa, Toru; Wei, Heng; Miano, Joseph M.; Abe, Jun-ichi; Berk, Bradford C.; Yan, Chen [Reprint Author]
CORPORATE SOURCE: Center for Cardiovascular Research, University of Rochester, 601 Elmwood Ave, Box 679, Rochester, NY, 14642, USA
chen_yan@urmc.rochester.edu
SOURCE: Circulation Research, (**September 5 2003**) Vol. 93, No. 5, pp. 406-413. print.
ISSN: 0009-7330 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Oct 2003
Last Updated on STN: 1 Oct 2003

AB **Atherosclerosis** involves cellular immune responses and altered vascular smooth muscle cell (VSMC) function. Nitric oxide (NO)/cGMP is uniquely capable of inhibiting key processes in **atherosclerosis**. In this study, we determined the effects of NO/cGMP and their molecular mechanisms in the regulation of NF-kappaB-dependent gene expression in VSMCs. We found that cGMP-elevating agents such as the NO donor S-nitroso-N-acetylpenicillamine (SNAP) and C-type natriuretic peptide (CNP), reduced TNF-alpha-induced NF-kappaB-dependent reporter gene expression in rat aortic VSMCs in a cGMP-dependent manner. The effects of SNAP and CNP on NF-kappaB are mediated by cAMP-dependent protein kinase (PKA) but not cGMP-dependent protein kinase (PKG) based on the findings that the selective PKA inhibitor, PKI, abolished the effects of SNAP and CNP on NF-kappaB, whereas the PKG inhibitor Rp-8-Br-PET-cGMP had no effect. Inhibition of cGMP-inhibited cAMP-hydrolyzing phosphodiesterase 3 (PDE3) blocked SNAP- and CNP-elicited effects on NF-kappaB-dependent transcription. Furthermore, cGMP analogues such as 8-pCPT-cGMP, which selectively activates PKG but does not inhibit PDE3, had no effect on NF-kappaB-mediated transcription. Activation of PKA by SNAP or cAMP-elevating agents not only inhibited TNF-alpha-induced NF-kappaB-dependent reporter gene expression but also reduced endogenous NF-kappaB-dependent adhesion molecule and chemokine expression. These results suggest that SNAP and CNP exert inhibitory effects on NF-kappaB-dependent transcription by activation of PKA via cGMP-dependent inhibition of PDE3 activity. Therefore, PDE3 is a novel mediator of inflammation in VSMCs.

CC Cytology - General 02502
Cytology - Animal 02506
Cytology - Human 02508
Genetics - General 03502
Genetics - Animal 03506
Genetics - Human 03508
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064

Enzymes - General and comparative studies: coenzymes 10802
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Endocrine - General 17002
Endocrine - Neuroendocrinology 17020
Muscle - Physiology and biochemistry 17504
Immunology - General and methods 34502

IT Major Concepts
Cardiovascular System (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics); Muscular System (Movement and Support)

IT Parts, Structures, & Systems of Organisms
aortic vascular smooth muscle cell: circulatory system, muscular system

IT Diseases
atherosclerosis: vascular disease, etiology, immunology
Arteriosclerosis (MeSH)

IT Chemicals & Biochemicals
C-type natriuretic peptide; NF-kappa-B [nuclear factor-kappa-B]; S-nitroso-N-acetylpenicillamine; TNF-alpha [tumor necrosis factor-alpha]; cGMP [cyclic GMP]; nitric oxide; phosphodiesterase-3 [EC 3.1.4.1]; protein kinase A [EC 2.7.1.37]

IT Methods & Equipment
gene expression analysis: genetic techniques, laboratory techniques

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 127830-04-0 (C-type natriuretic peptide)
79032-48-7 (S-nitroso-N-acetylpenicillamine)
7665-99-8 (cGMP)
7665-99-8 (cyclic GMP)
10102-43-9 (nitric oxide)
9036-21-9 (phosphodiesterase-3)
9025-82-5 (phosphodiesterase-3)
9036-21-9 (EC 3.1.4.1)
9025-82-5 (EC 3.1.4.1)
142008-29-5 (protein kinase A)
9026-43-1 (protein kinase A)
142008-29-5 (EC 2.7.1.37)
9026-43-1 (EC 2.7.1.37)

L76 ANSWER 29 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:480973 BIOSIS Full-text

DOCUMENT NUMBER: PREV200300480973
TITLE: VEGF-induced HUVEC migration and proliferation are decreased by PDE2 and PDE4 inhibitors.
AUTHOR(S): Favot, Laure; Keravis, Therese; Holl, Vincent; Le Bec, Alain; Lugnier, Claire [Reprint Author]
CORPORATE SOURCE: Pharmacologie et Physicochimie des Interactions Cellulaires et Moleculaires, Faculte de Pharmacie, CNRS UMR 7034, 74 Route du Rhin, Illkirch, 67401, France
claire@aspirine.u-strasbg.fr
SOURCE: Thrombosis and Haemostasis, (**August 2003**) Vol. 90, No. 2, pp. 334-343. print.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Oct 2003
Last Updated on STN: 15 Oct 2003

AB Migration and proliferation of endothelial cells in response to VEGF play an important role in angiogenesis associated to pathologies such as **atherosclerosis**, diabetes and tumor development. Elevation of cAMP in endothelial cells has been shown to inhibit growth factor-induced proliferation. Our hypothesis was that inactivation of cAMP-specific phosphodiesterases (PDEs) would inhibit angiogenesis. The purpose of this study was to evaluate the effect of PDE inhibitors on in vitro and in vivo angiogenesis, using human umbilical vein endothelial cell (HUVEC) and chick chorioallantoic membrane (CAM) models respectively. Here, we report that: 1) PDE2, PDE3, PDE4 and PDE5 are expressed in HUVEC; 2) EHNA (20 muM), PDE2 selective inhibitor, and RP73401 (10 muM), PDE4 selective inhibitor, are able to increase the intracellular cAMP level in HUVEC; 3) EHNA and RP73401 are able to inhibit proliferation, cell cycle progression and migration of HUVEC stimulated by VEGF; 4) these in vitro effects can be mimic by treating HUVEC with the cAMP analogue, 8-Br-cAMP (600 muM); 5) only the association of EHNA and RP73401 inhibits in vivo angiogenesis, indicating that both migration and proliferation must be inhibited. These data strongly suggest that PDE2 and PDE4 represent new potential therapeutic targets in pathological angiogenesis.

CC Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Endocrine - General 17002
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Development and Embryology - General and descriptive 25502
IT Major Concepts
Cardiovascular System (Transport and Circulation); Pharmacology
IT Parts, Structures, & Systems of Organisms
chorioallantoic membrane: embryonic structure
IT Chemicals & Biochemicals
8-Br-cAMP; EHNA: enzyme inhibitor-drug, PDE2 selective inhibitor; RP73401: enzyme inhibitor-drug, PDE4 selective inhibitor; VEGF [vascular endothelial growth factor]; cyclic AMP; phosphodiesterase 2: expression; phosphodiesterase 3: expression; phosphodiesterase 4: expression; phosphodiesterase 5: expression
IT Miscellaneous Descriptors
angiogenesis
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HUVEC cell line (cell line): human umbilical vein endothelial cells

Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 23583-48-4 (8-Br-cAMP)
144035-83-6 (RP73401)
127464-60-2 (VEGF)
127464-60-2 (vascular endothelial growth factor)
60-92-4 (cyclic AMP)
9040-59-9 (phosphodiesterase 2)
9036-21-9 (phosphodiesterase 3)
9036-21-9 (phosphodiesterase 4)
9068-52-4 (phosphodiesterase 5)

L76 ANSWER 30 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:42652 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300042652
TITLE: Arylalkanoyl pyridazines.
AUTHOR(S): Rochus, Jonas [Inventor, Reprint Author]; Beier, Norbert [Inventor]; Kluxen, Franz-Werner [Inventor]; Wolf, Michael [Inventor]
CORPORATE SOURCE: Darmstadt, Germany
ASSIGNEE: Merck Patent Gesellschaft Mit Beschraenkter Haftung, Germany
PATENT INFORMATION: US 6479494 20021112
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (**Nov 12 2002**) Vol. 1264, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003
AB Arylalkanoylpyridazine derivatives of the formula I ##STR1## and the physiologically acceptable salts thereof in which R1, R2, R3, R4, Q and B have the meanings given in Claim 1 act as phosphodiesterase IV inhibitors and can be employed for the treatment of osteoporosis, tumors, **atherosclerosis**, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, inflammatory processes, allergies, asthma, autoimmune diseases and AIDS.
NCL 514247000
CC Pathology - Therapy 12512
Metabolism - Metabolic disorders 13020
Cardiovascular system - Blood vessel pathology 14508
Respiratory system - Pathology 16006
Endocrine - Pancreas 17008
Bones, joints, fasciae, connective and adipose tissue - Pathology 18006
Nervous system - Pathology 20506
Pharmacology - General 22002
Pharmacology - Cardiovascular system 22010
Pharmacology - Connective tissue, bone and collagen-acting drugs 22012
Pharmacology - Endocrine system 22016
Pharmacology - Immunological processes and allergy 22018
Pharmacology - Respiratory system 22030
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
Immunology - Immunopathology, tissue immunology 34508
Allergy 35500
Medical and clinical microbiology - General and methods 36001
Chemotherapy - General, methods and metabolism 38502
Chemotherapy - Antiviral agents 38506
IT Major Concepts

Pharmacology
IT Diseases
AIDS: immune system disease, infectious disease, viral disease, drug therapy, acquired immunodeficiency syndrome
Acquired Immunodeficiency Syndrome (MeSH)
IT Diseases
allergy: immune system disease, drug therapy
Hypersensitivity (MeSH)
IT Diseases
asthma: immune system disease, respiratory system disease, drug therapy
Asthma (MeSH)
IT Diseases
atherosclerosis: vascular disease, drug therapy
Arteriosclerosis (MeSH)
IT Diseases
autoimmune disease: immune system disease, drug therapy
Autoimmune Diseases (MeSH)
IT Diseases
diabetes mellitus: endocrine disease/pancreas, metabolic disease, drug therapy
Diabetes Mellitus (MeSH)
IT Diseases
multiple sclerosis: immune system disease, nervous system disease, drug therapy
Multiple Sclerosis (MeSH)
IT Diseases
osteoporosis: bone disease, drug therapy
Osteoporosis (MeSH)
IT Diseases
rheumatoid arthritis: connective tissue disease, immune system disease, joint disease, drug therapy
Arthritis, Rheumatoid (MeSH)
IT Diseases
tumor: neoplastic disease, drug therapy
Neoplasms (MeSH)
IT Chemicals & Biochemicals
arylalkanoylpyridazine derivatives: antiallergic-drug, antiasthmatic-drug, antidiabetic-drug, antiinfective-drug, antiinflammatory-drug, antineoplastic-drug, antiviral-drug, cardiovascular-drug, enzyme inhibitor-drug, immunologic-drug; phosphodiesterase IV: inhibition; physiologically acceptable salts
IT Miscellaneous Descriptors
inflammatory processes
RN **9036-21-9** (phosphodiesterase IV)

L76 ANSWER 31 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:36012 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300036012
TITLE: Clinical manifestation of atherosclerotic peripheral arterial disease and the role of cilostazol in treatment of intermittent claudication.
AUTHOR(S): Crouse, John Robert [Reprint Author]; Allan, Michael C.; Elam, Marshall B.
CORPORATE SOURCE: Department of Medicine, Wake Forest University School of Medicine, Medical Center Boulevard, Winston Salem, NC, 27157, USA
SOURCE: Journal of Clinical Pharmacology, (**December 2002**) Vol. 42, No. 12, pp. 1291-1298. print.
CODEN: JCPCBR. ISSN: 0091-2700.

DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jan 2003
Last Updated on STN: 8 Jan 2003

AB Intermittent claudication (IC) is the symptomatic expression of peripheral arterial disease (PAD), which itself is a manifestation of systemic **atherosclerosis**. Like other forms of **atherosclerosis**, PAD is associated with elevated rates of cardiovascular and cerebrovascular morbidity and mortality. Until recently, therapeutic options for the treatment of the symptoms of IC have been limited, and the efficacy of available treatment has been questioned. Cilostazol, a selective phosphodiesterase III inhibitor with vasodilator, antiplatelet, and antiproliferative properties, has recently been approved for the treatment of IC symptoms in the United States. Cilostazol significantly improves maximal and pain-free walking distances. Clinical studies have also demonstrated that cilostazol favorably alters plasma lipids (elevates HDL-cholesterol, lowers triglycerides). These properties may contribute to the benefit of this drug in IC and in other diseases secondary to **atherosclerosis**.

CC Biochemistry studies - Lipids 10066
Biochemistry studies - Sterols and steroids 10067
Pathology - General 12502
Pathology - Diagnostic 12504
Pathology - Therapy 12512
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008
Pharmacology - Cardiovascular system 22010

IT Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences); Pharmacology

IT Diseases
atherosclerotic peripheral arterial disease: vascular disease, diagnosis, pathology

IT Diseases
intermittent claudication: vascular disease, drug therapy
Intermittent Claudication (MeSH)

IT Chemicals & Biochemicals
HDL-cholesterol [high density lipoprotein-cholesterol]; antiplatelet agents: cardiovascular-drug, hematologic-drug, efficacy, safety; cilostazol: antithrombotic-drug, cardiovascular-drug, enzyme inhibitor-drug, hematologic-drug; phosphodiesterase III; triglycerides

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 73963-72-1 (cilostazol)
9036-21-9 (phosphodiesterase III)

L76 ANSWER 32 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:313401 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200313401
TITLE: Impaired beta-agonist-dependent vasorelaxation following

balloon catheter de-endothelialization (BAL) is restored by cAMP phosphodiesterase (PDE3/4) inhibition.

AUTHOR(S): Smith, Carolyn Jean [Reprint author]; Rahman, Naziya [Reprint author]; Ding, Jia-Zhen; Moggio, Richard A.

CORPORATE SOURCE: Pathology, New York Medical College, Basic Sci Bldg BSB452, Valhalla, NY, 10595, USA

SOURCE: FASEB Journal, (**March 20, 2002**) Vol. 16, No. 4, pp. A217. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 29 May 2002
Last Updated on STN: 29 May 2002

AB Inhibition of cAMP PDE3 reduces **restenosis**. We previously found upregulation of PDE3A, 4B and 4D genes after BAL in rat aorta. The present studies examined whether cAMP-dependent vasorelaxation was impaired in aortic rings from controls (CON), or at 24Hr or 7Days after BAL. Maximal tone evoked by KCl or phenylephrine (PE), and PE sensitivity varied little after BAL. Isoproterenol (ISO) vasorelaxation of PE revealed beta-agonist subsensitivity: ISO EC50's were 300nM (CON) and 3muM (BAL7D); BAL24H did not relax at 10muM ISO. Preincubation with 0.1mM LNAME inhibited ISO in CON and BAL7D, but unexpectedly enhanced ISO in BAL24H (EC50 500nM). Inhibitors of PDE3 (0.3muM OPC3911) but not PDE4 (10muM Ro201724) reduced PE tone pre-ISO: OPC inhibited force by 30% (BAL7D or CON) to >67% (BAL24H). OPC enhanced the sensitivity to and efficacy for ISO (reversed LNAME effect) in all groups. In contrast, PDE4 inhibition improved ISO sensitivity only after BAL. PDE3/4 overexpression favors a growth-permissive/vasospastic state, which may affect vessel remodeling. Upregulation of specific vascular PDEs following angioplasty suggests a possible therapeutic target.

CC General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Pharmacology - General 22002
Pharmacology - Cardiovascular system 22010
Pharmacology - Neuropharmacology 22024

IT Major Concepts
Cardiovascular System (Transport and Circulation); Methods and Techniques; Pharmacology

IT Parts, Structures, & Systems of Organisms
aorta: circulatory system

IT Diseases
restenosis: vascular disease
Coronary **Restenosis** (MeSH)

IT Chemicals & Biochemicals
L-NAME [N-G-nitro-L-arginine methyl ester]; cAMP [cyclic AMP]; cAMP phosphodiesterase; isoproterenol: adrenergic agonist-drug, autonomic-drug, beta-adrenergic agonist-drug, cardiovascular-drug; phenylephrine: adrenergic agonist-drug, alpha-adrenergic agonist-drug, autonomic-drug; potassium chloride

IT Methods & Equipment
balloon catheter de-endothelialization: therapeutic method

IT Miscellaneous Descriptors

vasorelaxation; Meeting Abstract
RN 50903-99-6 (L-NAME)
50903-99-6 (N-G-nitro-L-arginine methyl ester)
60-92-4 (cAMP)
60-92-4 (cyclic AMP)
9036-21-9 (cAMP phosphodiesterase)
7683-59-2 (isoproterenol)
59-42-7 (phenylephrine)
7447-40-7 (potassium chloride)

L76 ANSWER 33 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:449863 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100449863
TITLE: Cilostazol represses vascular cell adhesion molecule-1 gene transcription via inhibiting NF-kappaB binding to its recognition sequence.
AUTHOR(S): Otsuki, Michio; Saito, Hiroshi; Xu, Xin; Sumitani, Satoru; Kouhara, Haruhiko; Kurabayashi, Masahiko; Kasayama, Soji [Reprint author]
CORPORATE SOURCE: Department of Molecular Medicine (C-4), Osaka University Graduate School of Medicine, 2-2 Yamada-oka, Suita-city, Osaka, 565-0871, Japan
kasayama@imed3.med.osaka-u.ac.jp
SOURCE: Atherosclerosis, (**September**, **2001**) Vol. 158, No. 1, pp. 121-128. print.
CODEN: ATHSBL. ISSN: 0021-9150.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Sep 2001
Last Updated on STN: 22 Feb 2002

AB Cilostazol is a specific inhibitor of cAMP phosphodiesterase, which is used for treatment of ischemic symptoms of peripheral vascular disease. Although cilostazol has antiplatelet and vasodilator properties, its effect on the expression of adhesion molecules in vascular endothelium is not known. In the present investigation, we examined the effect of cilostazol on the expression of vascular cell adhesion molecule-1 (VCAM-1) in cultured vascular endothelial cells. Cilostazol strongly inhibited tumor necrosis factor (TNF)-alpha-induced expression of VCAM-1 protein and its mRNA. In addition, cilostazol reduced TNF-alpha-induced U937 cell adhesion to the vascular endothelial cells. In transient transfection studies, cilostazol inhibited TNF-alpha-induced transcriptional activation of VCAM-1 promoter. Electrophoretic mobility shift assays revealed that cilostazol repressed TNF-alpha-induced increase in binding of the transcription nuclear factor-kappaB (NF-kappaB) to its recognition site of VCAM-1 promoter. Cilostazol, however, failed to prevent nuclear translocation of the NF-kappaB p65 protein. These data indicate that cilostazol repressed VCAM-1 gene transcription in cultured vascular endothelial cells, via inhibiting NF-kappaB binding to its recognition sequence. Since the expression of the adhesion molecule is one of the earliest events occurred in atherogenic process, cilostazol might have the potential to prevent **atherosclerosis** at least via inhibition of the expression of the adhesion molecule.

CC Cytology - Human 02508
Genetics - General 03502
Genetics - Human 03508
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Endocrine - General 17002

Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology; Cardiovascular System (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
endothelium
IT Diseases
atherosclerosis: vascular disease
Arteriosclerosis (MeSH)
IT Diseases
ischemia: vascular disease
Ischemia (MeSH)
IT Chemicals & Biochemicals
NF-kappa-B p65 protein [nuclear factor-kappa-B p65 protein]: transcription factor; TNF-alpha [tumor necrosis factor-alpha]; cAMP phosphodiesterase; cilostazol: anticoagulant-drug, enzyme inhibitor-drug, vasodilator-drug; mRNA [messenger RNA]; vascular cell adhesion molecule-1: expression
IT Methods & Equipment
electrophoretic mobility shift assay: analytical method, restriction fragment mapping
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HUVEC cell line: human umbilical vein endothelial cells
U937 cell line: human vascular endothelial cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN **9036-21-9** (cAMP phosphodiesterase)
73963-72-1 (cilostazol)
GEN human vascular cell adhesion molecule-1 gene (Hominidae): transcription repression

L76 ANSWER 34 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:175431 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200175431
TITLE: Altered phosphodiesterase 3 and phosphodiesterase 4 expression in "activated" neointimal cells: Potential therapeutic implications.
AUTHOR(S): Maurice, Donald Hector [Reprint author]; Dunkerley, Heather A.; Tilley, Douglas G.; Palmer, Daniel; Raymond, Daniel R.
CORPORATE SOURCE: Department of Pathology, Queen's University at Kingston, Botterell Hall, A221, Kingston, ON, K7L 3N6, Canada
SOURCE: Molecular Biology of the Cell, (**Dec.**, **2000**) Vol. 11, No. Supplement, pp. 233a. print.
Meeting Info.: 40th American Society for Cell Biology Annual Meeting. San Francisco, CA, USA. December 09-13, 2000. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Mar 2002
Last Updated on STN: 6 Mar 2002
CC General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506

Biochemistry studies - General 10060
Anatomy and Histology - Surgery 11105
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Muscle - Physiology and biochemistry 17504
IT Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
aorta: circulatory system; blood vessels: circulatory system; coronary artery: circulatory system; neointimal cells, activated; vascular smooth muscle cells: circulatory system, muscular system
IT Diseases
restenosis: vascular disease
Coronary **Restenosis** (MeSH)
IT Chemicals & Biochemicals
cyclic nucleotide phosphodiesterase; cyclic nucleotides; phosphodiesterase 3: altered expression; phosphodiesterase 4: altered expression
IT Methods & Equipment
balloon angioplasty: surgical method, therapeutic method
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN **9036-21-9Q** (cyclic nucleotide phosphodiesterase)
9040-59-9Q (cyclic nucleotide phosphodiesterase)
50812-31-2Q (cyclic nucleotide phosphodiesterase)
60098-35-3Q (cyclic nucleotide phosphodiesterase)
90910-07-9Q (cyclic nucleotide phosphodiesterase)

L76 ANSWER 35 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:43658 BIOSIS Full-text
DOCUMENT NUMBER: PREV199800043658
TITLE: Calmodulin-stimulated cyclic nucleotide phosphodiesterase (PDE1C) is induced in human arterial smooth muscle cells of the synthetic, proliferative phenotype.
AUTHOR(S): Rybalkin, Sergei D.; Bornfeldt, Karin E.; Sonnenburg, William K.; Rybalkina, Irina G.; Kwak, Keith S.; Hanson, Kim; Krebs, Edwin G.; Beavo, Joseph A. [Reprint author]
CORPORATE SOURCE: Dep. Pharmacol., Box 357280, Univ. Washington, Seattle, WA 98195, USA
SOURCE: Journal of Clinical Investigation, (**Nov. 15, 1997**) Vol. 100, No. 10, pp. 2611-2621. print.
CODEN: JCINAO. ISSN: 0021-9738.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jan 1998
Last Updated on STN: 27 Jan 1998
AB The diversity among cyclic nucleotide phosphodiesterases provides multiple mechanisms for regulation of cAMP and cGMP in the cardiovascular system. Here

we report that a calmodulin-stimulated phosphodiesterase (PDE1C) is highly expressed in proliferating human arterial smooth muscle cells (SMCS) in primary culture, but not in the quiescent SMCs of intact human aorta. High levels of PDE1C were found in primary cultures of SMCs derived from explants of human newborn and adult aortas, and in SMCs cultured from severe atherosclerotic lesions. PDE1C was the major cAMP hydrolytic activity in these SMCs. PDE expression patterns in primary SMC cultures from monkey and rat aortas were different from those from human cells. In monkey, high expression of PDE1B was found, whereas PDE1C was not detected. In rat SMCS, PDE1A was the only detectable calmodulin-stimulated PDE. These findings suggest that many of the commonly used animal species may not provide good models for studying the roles of PDEs in proliferation of human SMCs. More importantly, the observation that PDE1C is induced only in proliferating SMCs suggests that it may be both an indicator of proliferation and a possible target for treatment of **atherosclerosis** or **restenosis** after angioplasty, conditions in which proliferation of arterial SMCs is negatively modulated by cyclic nucleotides.

CC Cardiovascular system - General and methods 14501
Biochemistry studies - General 10060
Enzymes - General and comparative studies: coenzymes 10802

IT Major Concepts
Cardiovascular System (Transport and Circulation); Enzymology (Biochemistry and Molecular Biophysics)

IT Parts, Structures, & Systems of Organisms
aorta: circulatory system; arterial smooth muscle cells: circulatory system, muscular system, proliferation

IT Diseases
atherosclerosis: vascular disease
Arteriosclerosis (MeSH)

IT Chemicals & Biochemicals
calmodulin-stimulated cyclic nucleotide phosphodiesterase: induction

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: adult, newborn
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGN Classifier
Primates 86190
Super Taxa
Mammalia; Vertebrata; Chordata; Animalia
Organism Name
monkey
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Mammals, Nonhuman Vertebrates, Nonhuman Primates, Primates, Vertebrates

RN **9036-21-9Q** (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)
9040-59-9Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)
50812-31-2Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)

60098-35-3Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)
90910-07-9Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)

L76 ANSWER 36 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:72319 BIOSIS Full-text
DOCUMENT NUMBER: PREV199800072319
TITLE: Cilostazol, a cAMP phosphodiesterase inhibitor, attenuates the production of monocyte chemoattractant protein-1 in response to tumor necrosis factor-alpha in vascular endothelial cells.
AUTHOR(S): Nishio, Y.; Kashiwagi, A. [Reprint author]; Takahara, N.; Hidaka, H.; Kikkawa, R.
CORPORATE SOURCE: Third Dep. Med., Shiga Univ. Med. Sci., Seta, Ohtsu, Shiga 520-21, Japan
SOURCE: Hormone and Metabolic Research, (**Oct., 1997**) Vol. 29, No. 10, pp. 491-495. print.
CODEN: HMMRA2. ISSN: 0018-5043.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Feb 1998
Last Updated on STN: 24 Feb 1998

AB The induction of monocyte chemoattractant protein-1 (MCP-1) in vascular endothelial cells is thought to be an initial event in the development of atherosclerotic lesions. Therefore, inhibition of MCP-1 production may exhibit some effects in preventing **atherosclerosis**. in the present study, we found that 10 muM cilostazol, a cAMP phosphodiesterase inhibitor, increased the intracellular cAMP content by a twenty-five times of the basal level and resulted in the reduction of basal MCP-1 release by 41% from 168 +- 11 ng/24 hr/mg protein to 99 +- 14 ng/24 hr/mg protein (P<0.001) from cultured human umbilical vein endothelial cells. Furthermore, 10 muM cilostazol also significantly attenuated the dose-dependent increment of MCP-1 production by tumor necrosis factor-alpha. The inhibition was consistent with the reduction of MCP-1 mRNA level, possibly through reduced activation of transcription factor NF-kappaB level. Similarly, 1 mM dibutyryl cAMP inhibited MCP-1 production in endothelial cells. These data suggest that cilostazol inhibits MCP-1 production through increased intracellular cAMP levels and modulation of its expression in vascular endothelial cells.

CC Cardiovascular system - Anatomy 14502
Cytology - Human 02508
Biochemistry methods - Proteins, peptides and amino acids 10054
Metabolism - Carbohydrates 13004
Metabolism - Proteins, peptides and amino acids 13012
Cardiovascular system - Physiology and biochemistry 14504
Blood - Lymphatic tissue and reticuloendothelial system 15008
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Enzymes - Methods 10804
Physiology - Methods 12006
Pharmacology - Cardiovascular system 22010
Tissue culture, apparatus, methods and media 32500

IT Major Concepts
Cardiovascular System (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis)

IT Parts, Structures, & Systems of Organisms
vascular endothelial cells: circulatory system

IT Chemicals & Biochemicals
cilostazol: cyclic AMP phosphodiesterase inhibitor, pharmacological tool; monocyte chemoattractant protein-1; tumor necrosis factor-alpha

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HUVEC: human umbilical vein endothelial cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 73963-72-1 (cilostazol)
9025-82-5 (PHOSPHODIESTERASE)
9036-21-9 (CYCLIC AMP PHOSPHODIESTERASE)

L76 ANSWER 37 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:491589 BIOSIS Full-text
DOCUMENT NUMBER: PREV199799790792
TITLE: The effect of cilostazol, a cyclic nucleotide phosphodiesterase III inhibitor, on heparin-binding EGF-like growth factor expression in macrophages and vascular smooth muscle cells.
AUTHOR(S): Kayanoki, Yoshiro [Reprint author]; Che, Wenyi; Kawata, Sumio; Matsuzawa, Yuji; Higashiyama, Shigeki; Taniguchi, Naoyuki
CORPORATE SOURCE: Dep. Biochemistry, Osaka Univ. Med. Sch., Suita, Osaka 565, Japan
SOURCE: Biochemical and Biophysical Research Communications, (**1997**) Vol. 238, No. 2, pp. 478-481.
CODEN: BBRCA9. ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 1997
Last Updated on STN: 10 Dec 1997

AB Heparin-binding EGF-like growth factor (HB-EGF) is a mitogen for smooth muscle cells (SMC) and is detected in SMC and macrophages in atherosclerotic plaques, suggesting that HB-EGF may be associated with the pathogenesis of **atherosclerosis**. The present study indicates that cilostazol, a phosphodiesterase III inhibitor, suppresses the expression of HB-EGF in rat aortic SMC and in U-937 cells, a macrophage-like cell line, stimulated by lipopolysaccharide. Further, cilostazol diminished the induction of HB-EGF mRNA by methylglyoxal, which is a reactive dicarbonyl metabolite produced as the result of a glycation reaction and which might be associated with macroangiopathy caused by hyperglycemia. Cilostazol suppressed the production of HB-EGF protein in the conditioned medium of SMC. These data suggest that cilostazol might act by suppressing the progression of atherogenesis by means of suppressing the expression of HB-EGF in SMC and macrophages.

CC Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Biophysics - Molecular properties and macromolecules 10506
Enzymes - Physiological studies 10808
Pathology - Therapy 12512
Metabolism - Carbohydrates 13004
Metabolism - Proteins, peptides and amino acids 13012
Metabolism - Nucleic acids, purines and pyrimidines 13014
Metabolism - Metabolic disorders 13020
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508

Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Blood - Lymphatic tissue and reticuloendothelial system 15008
Endocrine - General 17002
Muscle - Physiology and biochemistry 17504
Muscle - Pathology 17506
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Blood and hematopoietic agents 22008
Pharmacology - Cardiovascular system 22010
Pharmacology - Endocrine system 22016
Pharmacology - Muscle system 22022

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Cardiovascular System (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Hematology (Human Medicine, Medical Sciences); Metabolism; Muscular System (Movement and Support); Pharmacology

IT Chemicals & Biochemicals
CILOSTAZOL; CYCLIC NUCLEOTIDE PHOSPHODIESTERASE

IT Miscellaneous Descriptors
ANTI-PLATELET AGENT; AORTIC SMOOTH MUSCLE CELLS; ATHEROGENESIS; **ATHEROSCLEROSIS**; ATHEROSCLEROTIC PLAQUES; BLOOD AND LYMPHATICS; CARDIOVASCULAR SYSTEM; CILOSTAZOL; CIRCULATORY SYSTEM; CYCLIC NUCLEOTIDE PHOSPHODIESTERASE III; CYCLIC NUCLEOTIDE PHOSPHODIESTERASE III INHIBITOR; EXPRESSION; HEPARIN-BINDING EGF-LIKE GROWTH FACTOR; HEPARIN-BINDING EGF-LIKE GROWTH FACTOR MRNA; HEPARIN-BINDING EPIDERMAL GROWTH FACTOR-LIKE GROWTH FACTOR; HEPARIN-BINDING EPIDERMAL GROWTH FACTOR-LIKE GROWTH FACTOR MESSENGER RNA; HYPERGLYCEMIA; MACROANGIOPATHY; MACROPHAGE-LIKE CELLS; MACROPHAGES; METABOLIC DISEASE; MITOGEN; MUSCULAR SYSTEM; PATHOGENESIS; PHARMACOLOGY; VASCULAR DISEASE; VASCULAR SMOOTH MUSCLE CELLS; 6-(4-(1-CYCLOHEXYL-1H-TETRAZOL-5-YL)-BUTOXY)-3,4-DIHYDRO-2-(1H)-QUINOLINONE

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
U-937: cell line
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 73963-72-1 (CILOSTAZOL)
9036-21-9Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)
9040-59-9Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)
50812-31-2Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)
60098-35-3Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)
90910-07-9Q (CYCLIC NUCLEOTIDE PHOSPHODIESTERASE)

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ACCESSION NUMBER: 1997:24643 BIOSIS Full-text
DOCUMENT NUMBER: PREV199799323846
TITLE: Effect of cilostazol, a cAMP phosphodiesterase inhibitor, on nitric oxide production by vascular smooth muscle cells.
AUTHOR(S): Ikeda, Uichi [Reprint author]; Ikeda, Michiyo; Kano, Shogo; Kanbe, Toshiko; Shimada, Kazuyuki
CORPORATE SOURCE: Dep. Cardiol., Jichi Med. Sch., Minamikawachi-Machi, Tochigi 329-04, Japan
SOURCE: European Journal of Pharmacology, (**1996**) Vol. 314, No. 1-2, pp. 197-202.
CODEN: EJPHAZ. ISSN: 0014-2999.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jan 1997
Last Updated on STN: 23 Jan 1997

AB We investigated the effects of cilostazol, a cAMP phosphodiesterase inhibitor, on nitric oxide (NO) synthesis in cultured rat vascular smooth muscle cells. Incubation of the cultures with interleukin-1-beta (10 ng/ml) for 24 h caused a significant increase in the accumulation of nitrite, a stable metabolite of NO. Although cilostazol by itself showed no effect on nitrite accumulation, it stimulated interleukin-1-beta- induced nitrite accumulation in a concentration-dependent manner (10-8-10-5 M). This effect of cilostazol was completely abolished in the presence of N-G-monomethyl-L-arginine, actinomycin D or dexamethasone. The cilostazol-induced nitrite production was accompanied by increased inducible NO synthase protein expression. In the presence of dibutyryl-cAMP, interleukin-1-beta-induced nitrite accumulation was further increased, but the stimulatory effect of cilostazol on nitrite accumulation was blunted. The effect of cilostazol was also abolished in the presence of Rp-8-bromoadenosine-3',5'-cyclic monophosphorothioate, a competitive inhibitor of protein kinase A. Addition of cilostazol to the cultures significantly increased intracellular cAMP levels of vascular smooth muscle cells. These results indicate that cilostazol increases NO synthesis in interleukin-1-beta-stimulated vascular smooth muscle cells, at least partially through a cAMP-dependent pathway.

CC Cytology - Animal 02506
Biochemistry - Gases 10012
Biophysics - Molecular properties and macromolecules 10506
Enzymes - Physiological studies 10808
Pathology - Therapy 12512
Metabolism - General metabolism and metabolic pathways 13002
Cardiovascular system - Physiology and biochemistry 14504
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Muscle - Anatomy 17502
Muscle - Physiology and biochemistry 17504
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Cardiovascular system 22010

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular System (Transport and Circulation); Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Muscular System (Movement and Support); Pharmacology

IT Chemicals & Biochemicals
CILOSTAZOL; PHOSPHODIESTERASE; NITRIC OXIDE; CYCLIC AMP PHOSPHODIESTERASE; NITRITE; NITRIC OXIDE SYNTHASE

IT Miscellaneous Descriptors
ANTIATHEROGENIC-DRUG; **ATHEROSCLEROSIS**; CARDIOVASCULAR SYSTEM; CILOSTAZOL; CYCLIC AMP PHOSPHODIESTERASE INHIBITOR; INDUCIBLE ACTIVITY; INTERLEUKIN-1; MUSCULAR SYSTEM; NITRIC OXIDE; NITRIC OXIDE PRODUCTION;

NITRIC OXIDE SYNTHASE; NITRITE; PHARMACODYNAMICS; PHARMACOLOGY; PLATELET AGGREGATION INHIBITOR; VASCULAR DISEASE; VASCULAR SMOOTH MUSCLE CELLS; VASCULAR SYSTEM

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 73963-72-1 (CILOSTAZOL)
9025-82-5 (PHOSPHODIESTERASE)
10102-43-9 (NITRIC OXIDE)
9036-21-9 (CYCLIC AMP PHOSPHODIESTERASE)
14797-65-0 (NITRITE)
125978-95-2 (NITRIC OXIDE SYNTHASE)

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ACCESSION NUMBER: 1993:372968 BIOSIS Full-text
DOCUMENT NUMBER: PREV199396058643
TITLE: ADH resistance of LLC-PK-1 cells caused by overexpression of cAMP-phosphodiesterase type-IV.
AUTHOR(S): Yamaki, Mario; McIntyre, Steven; Murphy, Josie M.; Swinnen, Johannes V.; Conti, Marco; Dousa, Thomas P. [Reprint author]
CORPORATE SOURCE: Mayo Clinic Foundation, 901 Guggenheim Building, 200 First St., SW, Rochester, MN 55905, USA
SOURCE: Kidney International, (**1993**) Vol. 43, No. 6, pp. 1286-1297.
CODEN: KDYIA5. ISSN: 0085-2538.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 1993
Last Updated on STN: 28 Sep 1993

AB The studies of animal models of nephrogenic diabetes insipidus (NDI) suggest that abnormally high activity of cAMP phosphodiesterase (cAMP-PDE) may cause unresponsiveness to the diuretic effect of AVP. We explored whether overexpression of one of the cAMP-PDE type isozymes, PDE-IV, in (8-Arg)-vasopressin (AVP) sensitive renal epithelial LLC-PK-1 cells can prevent the hormone-elicited cAMP increase. LLC-PK-1 cells were stably transfected with ratPDE3.1 cDNA (which encodes for rolipram-Sensitive PDE-IV), inserted in plasmid pCMV5 and then were compared with sham-transfected LLC-PK-1 cells and the wild LLC-PK-1 cells. In the stably transfected clone (LLC-PK-1-S 16), the rolipram-sensitive PDE-IV activity was about five times higher than in controls, whereas activities of other types of PDEs were not different. The presence of cognate mRNA for PDE-IV was confirmed by Northern blot. Whereas in the control cells (wild LLC-PK-1 cells and sham-transfected LLC-PK-1 cells), the incubation with 10-7 M AVP increased cAMP more than tenfold, the LLC-PK-1-S 16 cells with overexpressed cAMP-PDE were resistant to cAMP-increasing effects of AVP and forskolin. However, in the same LLC-PK-1-S 16 cells the cGMP increases in response to nitroprusside were not diminished. The AVP-dependent cAMP accumulation in LLC-PK-1-S 16 cells with overexpressed PDE-IV was restored by addition of roliprams which decreased cAMP-PDE activity to the levels similar to those in wild LLC-PK-1 cells and sham-transfected LLC-PK-1- A1 cells. In contrast, inhibitors of other PDE isozymes (PDE-I or PDE-III) had little or no effect. Our findings show that excessive activity of cAMP-PDE, in this case of isozyme PDE-IV, can cause resistance to AVP which

is analogous to that observed in collecting ducts of mice with hereditary nephrogenic diabetes insipidus.

CC Cytology - Animal 02506
Genetics - Animal 03506
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Carbohydrates 10068
Enzymes - Physiological studies 10808
Metabolism - Carbohydrates 13004
Metabolism - Metabolic disorders 13020
Urinary system - Pathology 15506
Endocrine - Pancreas 17008

IT Major Concepts
Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Genetics; Metabolism; Urinary System (Chemical Coordination and Homeostasis)

IT Chemicals & Biochemicals
CAMP-PHOSPHODIESTERASE; CYCLIC AMP; ALCOHOL DEHYDROGENASE

IT Miscellaneous Descriptors
ATHEROSCLEROSIS; HYPERCHOLESTEROLEMIA

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN **9036-21-9** (CAMP-PHOSPHODIESTERASE)
60-92-4 (CYCLIC AMP)
9031-72-5 (ALCOHOL DEHYDROGENASE)

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ACCESSION NUMBER: 1993:144841 BIOSIS Full-text
DOCUMENT NUMBER: PREV199395077641
TITLE: Effect of cilostazol, a cyclic AMP phosphodiesterase inhibitor, on the proliferation of rat aortic smooth muscle cells in culture.
AUTHOR(S): Takahashi, Sadao; Oida, Koji [Reprint author]; Fujiwara, Ryuichi; Maeda, Hajime; Hayashi, Shinta; Takai, Shirotada; Tamai, Toshitaka; Nakai, Tsuguhiko; Miyabo, Susumu
CORPORATE SOURCE: Third Dep. Intern. Med., Fukui Med. Sch., 23 Shimoaizuki, Matsuoka-Cho, Fukui 910-11, Japan
SOURCE: Journal of Cardiovascular Pharmacology, (**1992**) Vol. 20, No. 6, pp. 900-906.
CODEN: JCPCDT. ISSN: 0160-2446.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Mar 1993
Last Updated on STN: 17 Mar 1993

AB Cilostazol, a cyclic AMP phosphodiesterase inhibitor, has been used as an antiplatelet agent. In the present study, we investigated the in vitro effect of cilostazol on DNA synthesis in rat aortic arterial smooth muscle cells (SMCs) in culture stimulated with fetal calf serum (FCS), platelet-derived growth factor (PDGF), insulin, or insulin-like growth factor-I (IGF-I). Micromolar concentrations of cilostazol inhibited (3H)thymidine incorporation into DNA and cell growth as determined by cell number and protein concentration. Treatment with cilostazol increased the intracellular concentration of cyclic AMP, suggesting that the inhibition of SMC

proliferation by cilostazol may be mediated through increased levels of cyclic AMP. The results suggested that cilostazol, by interfering with the proliferation of arterial SMCs, may have potential to prevent initiation and progression of **atherosclerosis**.

CC Cytology - Animal 02506
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - Physiological studies 10808
Pathology - Therapy 12512
Metabolism - Proteins, peptides and amino acids 13012
Metabolism - Nucleic acids, purines and pyrimidines 13014
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood cell studies 15004
Endocrine - General 17002
Endocrine - Pancreas 17008
Muscle - Physiology and biochemistry 17504
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Cardiovascular system 22010
Pharmacology - Muscle system 22022

IT Major Concepts
Cardiovascular System (Transport and Circulation); Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Muscular System (Movement and Support); Pharmacology

IT Chemicals & Biochemicals
CILOSTAZOL; CYCLIC AMP PHOSPHODIESTERASE; THYMIDINE; CYCLIC AMP; INSULIN-LIKE GROWTH FACTOR-I

IT Miscellaneous Descriptors
ANTIATHEROGENIC-DRUG; **ATHEROSCLEROSIS**; CYCLIC AMP; DNA METABOLISM; ENZYME INHIBITOR-DRUG; INSULIN-LIKE GROWTH FACTOR-I; PHARMACODYNAMICS; PHARMACOKINETICS; PLATELET-DERIVED GROWTH FACTOR; SERUM; THYMIDINE

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Muridae
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 73963-72-1 (CILOSTAZOL)
9036-21-9 (CYCLIC AMP PHOSPHODIESTERASE)
50-89-5 (THYMIDINE)
60-92-4 (CYCLIC AMP)
67763-96-6 (INSULIN-LIKE GROWTH FACTOR-I)

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ACCESSION NUMBER: 1993:7898 BIOSIS Full-text
DOCUMENT NUMBER: PREV199395007898
TITLE: Inhibition of pig aortic smooth muscle cell DNA synthesis by selective type III and type IV cyclic AMP phosphodiesterase inhibitors.
AUTHOR(S): Souness, John E. [Reprint author]; Hassall, Giles A.; Parrott, David P.
CORPORATE SOURCE: Dagenham Res. Centre, Rhone-Poulenc Rorer Ltd., Rainham Road South, Dagenham, Essex RM10 7XS, UK
SOURCE: Biochemical Pharmacology, (**1992**) Vol. 44, No. 5, pp. 857-866.

CODEN: BCPCA6. ISSN: 0006-2952.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1992
Last Updated on STN: 10 Feb 1993

AB Foetal calf serum (FCS) and platelet-derived growth factor (PDGF)-stimulated incorporation of (3H)thymidine into pig aortic smooth muscle cell (ASMC) DNA was decreased by agents that either stimulated the synthesis (forskolin) or inhibited the breakdown (3-isobutyl-1- methylxanthine, IBMX) of cAMP. FCS-stimulated incorporation of (3H)thymidine into DNA was also reduced by selective inhibitors of cAMP-specific phosphodiesterase (PDE IV) (Ro-20-1724, rolipram) and cGMP-inhibited cAMP PDE (PDE III) (SK&F 94836). IBMX, Ro-20-1724, rolipram and SK&F 94836 enhanced forskolin inhibition of DNA synthesis. Alone, rolipram was a relatively weak inhibitor of FCS-induced ASMC DNA synthesis (IC-25 gt 20 mu-M); however, in the presence of a threshold concentration of SK&F 94836 (20 mu-M), the potency of rolipram increased (IC-25 = 4 mu-M), suggesting synergy in the actions of PDE III and PDE IV inhibitors. SK&F 94836 and rolipram elicited 30% and 37%, respectively, reductions in FCS-induced ASMC proliferation and potentiated the inhibitory actions of forskolin. PDE III and PDE IV inhibitors alone, exerted minimal effects on ASMC cAMP levels after a short term (10 min) or long-term (2 or 24 hr) exposure, but enhanced forskolin-induced accumulation of cAMP. ASMC spontaneously released cAMP into the extracellular medium, a process that was increased by forskolin. PDE III and PDE IV inhibitors had no effect alone on cAMP extrusion but enhanced the effect of forskolin. Exposure of ASMC to forskolin or SK&F 94836 for 15 min increased the activity ratio (AR) of cAMP-dependent protein kinase from 0.05 to 0.17 and 0.23, respectively. Ro-20-1724, alone, did not affect cAMP-dependent protein kinase but enhanced the stimulatory effect of forskolin (AR = 0.37) and SK&F 94836 (AR = 0.27). Agents that increased cGMP synthesis (glycerol trinitrate, atrial natriuretic factor) or decrease its hydrolysis by selectively inhibiting cGMP-specific PDE (PDE V) (zaprinast) exerted no effects on FCS- or PDGF-stimulated (3H)thymidine incorporation into DNA either alone or in combination. The cytosolic fraction of pig ASMC contained four cyclic nucleotide PDEs which were categorized as PDE V, Ca-2+/calmodulin-stimulated PDE (PDE I), PDE III and PDE IV. PDE I and III activities were also associated with the particulate fraction. The results demonstrate that inhibitors of PDEs III and IV alone or in combination with forskolin, reduce ASMC DNA synthesis and proliferation, through an action likely to involve elevation of intracellular cAMP. In contrast, inhibition of cGMP hydrolysing PDE subtypes (I and V) exerted no effect on DNA synthesis in this cell type.

CC Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - Physiological studies 10808
Metabolism - Nucleic acids, purines and pyrimidines 13014
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Cardiovascular system 22010
IT Major Concepts
Cardiovascular System (Transport and Circulation); Metabolism; Pharmacology
IT Chemicals & Biochemicals
CYCLIC AMP PHOSPHODIESTERASE; RO-20-1724; ROLIPRAM; SKF-94836; 3-ISOBUTYL-1-METHYLXANTHINE; FORSKOLIN; CYCLIC GMP
IT Miscellaneous Descriptors
ATHEROSCLEROSIS; CYCLIC GMP; ENZYME INHIBITOR; FORSKOLIN; RO-20-1724; ROLIPRAM; SKF-94836; 3=ISOBUTYL-1-METHYLXANTHINE
ORGN Classifier
Suidae 85740

Super Taxa
Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Suidae
Taxa Notes
Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
RN **9036-21-9** (CYCLIC AMP PHOSPHODIESTERASE)
29925-17-5 (RO-20-1724)
61413-54-5 (ROLIPRAM)
115344-47-3 (SKF-94836)
28822-58-4 (3-ISOBUTYL-1-METHYLXANTHINE)
66575-29-9 (FORSKOLIN)
7665-99-8 (CYCLIC GMP)

L76 ANSWER 42 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1992:329874 BIOSIS Full-text
DOCUMENT NUMBER: PREV199294031715; BA94:31715
TITLE: EFFECTS OF THE ANTI-PLATELET AGENT CILOSTAZOL ON PERIPHERAL VASCULAR DISEASE IN PATIENTS WITH DIABETES MELLITUS.
AUTHOR(S): UCHIKAWA T [Reprint author]; MURAKAMI T; FURUKAWA H
CORPORATE SOURCE: DEP INTERNAL MED, TOKYO METROPOLITAN KOMAGOME HOSP, 3-18-22 HONKOMAGOME, BUNKYO-KU, TOKYO 113
SOURCE: Arzneimittel-Forschung, (**1992**) Vol. 42, No. 3, pp. 322-324.
CODEN: ARZNAD. ISSN: 0004-4172.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 11 Jul 1992
Last Updated on STN: 10 Sep 1992

AB Effects of cilostazol (OPC-13013, CAS 73963-72-1), a selective inhibitor of platelet cAMP-phosphodiesterase, on peripheral vascular disease in diabetes mellitus were studied. Cilostazol in a dose of 200 to 300 mg/d was administered to 5 diabetic patients with **arteriosclerosis** obliterans. Skin temperature of the finger and the toe, which reflects blood flow to the tissue, was selected as an objective index of cilostazol effects and measured by infra-red thermography at a constant temperature of 26° C. Before administration, digital skin temperatures were low in 9 limbs of 5 patients. 200 mg/d of cilostazol significantly ($p < 0.001$) increased the digital skin temperatures of 8 limbs, the increase (mean ± SD) ranging from 29.9 ± 1.4° C to 33.2° C ± 1.2 ° C for the average skin temperatures and from 28.7 ± 2.1° C to 33.1 ± 1.5° C for the lowest ones. An increase in the dose to 300 mg/d resulted in further elevation of skin temperatures of the digits. Cilostazol constantly elicited an increase in blood flow to the digits within the range of its therapeutic dose. This effect was observed about 1 month after initiation of administration and persisted while administration was continued. The measurement of digital skin temperatures by infrared thermography provided a noninvasive means to individualize the dosage of cilostazol and to monitor the cilostazol effect and patient compliance during long-term administration. It is concluded that cilostazol exerts a potent and steady vasodilatory effect on peripheral circulation in patients with diabetes mellitus.

CC Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Enzymes - Physiological studies 10808
Metabolism - Carbohydrates 13004
Metabolism - Proteins, peptides and amino acids 13012
Metabolism - Metabolic disorders 13020

Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Endocrine - Pancreas 17008
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008
Temperature - General measurement and methods 23001

IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Cardiovascular System (Transport and Circulation); Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Methods and Techniques; Pharmacology

IT Miscellaneous Descriptors
HUMAN ENZYME INHIBITOR-DRUG CYCLIC AMP PHOSPHODIESTERASE BLOOD FLOW VASODILATION THERMOGRAPHY

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 73963-72-1 (CILOSTAZOL)
9036-21-9 (CYCLIC AMP PHOSPHODIESTERASE)

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ACCESSION NUMBER: 1990:455499 BIOSIS Full-text
DOCUMENT NUMBER: PREV199090106139; BA90:106139
TITLE: THE STIMULATORY EFFECT OF HEAVY METAL CATIONS ON PROLIFERATION OF AORTIC SMOOTH MUSCLE CELLS.
AUTHOR(S): LU K-P [Reprint author]; ZHAO S-H; WANG D-S
CORPORATE SOURCE: RES DEP CELL REGUL, XUZHOU MED COLL, XUZHOU 221002, CHINA
SOURCE: Science in China Series B Chemistry Life Sciences and Earth Sciences, (**1990**) Vol. 33, No. 3, pp. 303-310.
CODEN: SCBSE5. ISSN: 1001-652X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 Oct 1990
Last Updated on STN: 7 Oct 1990

AB Heavy metal cations Cd2+, Pb2+, and Hg2+ were added to substitute for Ca2+ in culture media to study their effect on the relationship between CaM and the proliferation of cultured rabbit aortic smooth muscle cells (ASMC). It was found that all the heavy metal cations studied stimulated the proliferation of ASMC in varying degrees, increased the CaM content in cells at late G1 stage and decreased the activity of cAMP PDE. These results suggest that the adverse effect of heavy metals may be related to the pathogenesis of **atherosclerosis** and hypertensive disease.

CC Cytology - Animal 02506
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Minerals 10069
Enzymes - Physiological studies 10808
Cardiovascular system - Blood vessel pathology 14508
Toxicology - Environment and industry 22506
Public health - Air, water and soil pollution 37015

IT Major Concepts
Cardiovascular System (Transport and Circulation); Cell Biology;

Enzymology (Biochemistry and Molecular Biophysics); Pollution Assessment Control and Management; Toxicology

IT Miscellaneous Descriptors
RABBIT CADMIUM LEAD MERCURY **ATHEROSCLEROSIS** HYPERTENSION CYCLIC AMP PHOSPHODIESTERASE CALMODULIN ENVIRONMENTAL TOXICOLOGY POLLUTION

ORGN Classifier
Leporidae 86040
Super Taxa
Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

RN 7440-43-9 (CADMIUM)
7439-92-1 (LEAD)
7439-97-6 (MERCURY)
9036-21-9 (CYCLIC AMP PHOSPHODIESTERASE)

L76 ANSWER 44 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1977:198142 BIOSIS Full-text
DOCUMENT NUMBER: PREV197764020506; BA64:20506
TITLE: ANNALS OF THE NEW-YORK ACADEMY OF SCIENCES VOL 275 ATHEROGENESIS.
AUTHOR(S): CAMERINI-DAVALOS R A; ET AL
SOURCE: (**1976**) pp. 390. Annals of the New York Academy of Sciences.
Publisher: Series: Annals of the New York Academy of Sciences.
ISSN: 007-8923.
DOCUMENT TYPE: Book
Conference; (Meeting)
FILE SEGMENT: BA
LANGUAGE: Unavailable

AB Contributors discuss such topics as flow at interfaces, macro- and microrheology, experimental thrombosis, endothelial surface charge, contractile and relaxing proteins, human atherosclerotic plaques, collagen formation, neural factors, protein-lipoprotein interactions, low-density lipoproteins and apolipoproteins. Repair responses and tissue lipid, lipoprotein uptake and degradation, immunologic arterial injury, cholesterol ester metabolism, arterial endothelial cells, arterial wall cell and sclerogenesis, vessel wall metabolism, cyclic[c]AMP and cAMP phosphodiesterase, cholesterol and atherosclerotic lesions, inherited vasculopathy, atherosclerotic regression and occlusive **atherosclerosis** are also discussed. Numerous micrographs supplement the text. Each group of papers is followed by a discussion section. Individual papers are indexed in BIORESEARCH INDEX.

CC General biology - Symposia, transactions and proceedings 00520
Methods - Photography 01012
Cytology - Human 02508
Genetics - Human 03508
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biochemistry studies - Sterols and steroids 10067
Biophysics - General 10502
Enzymes - Physiological studies 10808
Anatomy and Histology - Regeneration and transplantation 11107
Movement 12100
Metabolism - Lipids 13006

Metabolism - Sterols and steroids 13008
Metabolism - Nucleic acids, purines and pyrimidines 13014
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
Bones, joints, fasciae, connective and adipose tissue - Physiology and biochemistry 18004
Bones, joints, fasciae, connective and adipose tissue - Pathology 18006
Nervous system - Physiology and biochemistry 20504
Immunology - General and methods 34502

IT Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences)

IT Miscellaneous Descriptors
BOOK SYMPOSIUM HUMAN CHOLESTEROL ESTER PROTEIN LIPO PROTEIN INTERACTION COLLAGEN CYCLIC AMP CYCLIC AMP PHOSPHO DI ESTERASE INHERITED VASCULOPATHY ATHERO SCLEROSIS SCLEROGENESIS IMMUNOLOGIC ARTERIAL INJURY

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 57-88-5 (CHOLESTEROL)
60-92-4 (CYCLIC AMP)
9036-21-9 (CYCLIC AMP PHOSPHO DI ESTERASE)

L76 ANSWER 45 OF 57 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001101896 EMBASE Full-text
TITLE: Cilostazol: Treatment of intermittent claudication.
AUTHOR: Reilly M.P.; Mohler III E.R.
CORPORATE SOURCE: Dr. E.R. Mohler III, Department of Medicine, School of Medicine, University of Pennsylvania, 51 North 39th St., Philadelphia, PA 19104-2699, United States. emmd@mail.med.upenn.edu
SOURCE: Annals of Pharmacotherapy, (2001) Vol. 35, No. 1, pp. 48-56. .
Refs: 60
ISSN: 1060-0280 CODEN: APHRER
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English; Spanish; French
ENTRY DATE: Entered STN: 6 Apr 2001
Last Updated on STN: 6 Apr 2001

AB OBJECTIVE: To review the pharmacology and clinical utility of cilostazol, an antiplatelet and vasodilator agent approved for the management of intermittent claudication. DATA SOURCES: Primary literature on cilostazol was identified from a comprehensive MEDLINE literature search (1980-February 2000). Selected meeting abstracts and manufacturer literature were also used as source material. Indexing terms included cilostazol, intermittent claudication, platelet inhibitors, and **restenosis**. STUDY SELECTION: Human clinical, pharmacokinetic and randomized comparative trials performed in the US and Asia were reviewed. Selected in vitro, ex vivo, and animal studies were evaluated when human data were not available. DATA SYNTHESIS: Intermittent claudication, defined as reproducible discomfort of a muscle group induced by exercise and relieved by rest, is the most common clinical manifestation of peripheral arterial disease (PAD). Cilostazol, a specific inhibitor of cyclic

adenosine monophosphate phosphodiesterase in platelets and vascular smooth-muscle cells, is a potent antiplatelet agent and vasodilator that reduces vascular proliferation and has lipid-lowering effects in vivo. Recent multicenter, randomized, placebo-controlled trials have led to approval of cilostazol by the Food and Drug Administration for relief of intermittent claudication in patients with stable PAD. Cilostazol doubled walking distances and improved quality of life compared with placebo in these studies. One trial found that cilostazol was more effective than pentoxifylline, the only alternative pharmacologic therapy for claudication. Although frequent (.apprx.50%) minor adverse effects, including headache, diarrhea, and palpitations, may occur in clinical practice, cilostazol has not been associated with major adverse events or increased mortality. Small, nonblind studies suggest that cilostazol may prove useful in preventing thrombosis and **restenosis** following percutaneous coronary interventions, although these remain unlabeled uses. CONCLUSIONS: The unique combination of antiplatelet, vasodilatory, and antiproliferative effects of cilostazol appear to make it an attractive agent for use in patients with PAD. Clinical trials demonstrating a significant improvement in walking distances with cilostazol therapy suggest that it will be an important tool in improving symptoms and quality of life in patients with intermittent claudication.

CT Medical Descriptors:
*intermittent claudication: DT, drug therapy
artery disease: DT, drug therapy
vasodilatation
restenosis: DT, drug therapy
restenosis: PC, prevention
thrombocyte aggregation inhibition
quality of life
headache: SI, side effect
diarrhea: SI, side effect
heart palpitation: SI, side effect
thrombosis: DT, drug therapy
area under the curve
human
clinical trial
meta analysis
review
priority journal
Drug Descriptors:
*cilostazol: AE, adverse drug reaction
*cilostazol: CM, drug comparison
*cilostazol: DO, drug dose
*cilostazol: DT, drug therapy
*cilostazol: PK, pharmacokinetics
*cilostazol: PD, pharmacology
*pentoxifylline: CM, drug comparison
cyclic AMP phosphodiesterase

RN (cilostazol) 73963-72-1; (pentoxifylline) 6493-05-6; (cyclic AMP phosphodiesterase) **9036-21-9**

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ACCESSION NUMBER: 1999377105 EMBASE Full-text
TITLE: Optimal duration of cilostazol treatment to prevent intimal thickening after stent implantation.
AUTHOR: Tanaka T.; Oka Y.; Sada T.; Kira Y.
CORPORATE SOURCE: Dr. T. Tanaka, Department of Cardiology, Showa General Hospital, 2-450 Tenjin-cho, Kodaira-shi, Tokyo 187-8510, Japan
SOURCE: Japanese Journal of Interventional Cardiology, (1999) Vol.

14, No. 5, pp. 433-437. .
Refs: 17
ISSN: 0914-8922 CODEN: JJICFB
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 014 Radiology
018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
ENTRY DATE: Entered STN: 18 Nov 1999
Last Updated on STN: 18 Nov 1999

AB Background: Cilostazol reportedly prevents smooth cell proliferation after coronary stenting. Purpose(s): To determine the optimal period of cilostazol administration for the prevention of intimal thickening after coronary stent implantation. Methods: Intimal thickening was evaluated in 118 patients (pts) undergoing Palmaz-Schatz stent implantation divided randomly into 4 groups: G1 (cilostazol 200 mg/day for 1 month), G3 (for 3 months), G6 (for 6 months), and C (ticlopidine 200 mg/day for 6 months instead of cilostazol). All pts were given aspirin (280 mg/day for 6 months). Follow-up coronary angiography was obtained 6 months after stenting, and analyzed quantitatively. Results: There were no differences in reference vessel diameter, minimal luminal diameter (MLD) nor % diameter stenosis (%DS) between the 4 groups before stenting. However 6 months later, the MLD was significantly bigger ($p<0.01$), the %DS lower ($p<0.01$) in both G3 and G6, and the late loss also lower (G3=$p<0.05$; G6=$p<0.01$) compared to G1. There were no significant differences between the G3 and G6, nor G3 and C groups. **Restenosis** rate and need for target lesion revascularization did not differ among the 4 groups. Conclusions: Three month administration of cilostazol seems to prevent intimal thickening, but is not effective in preventing **restenosis** after Palmaz-Schatz stent implantation.

CT Medical Descriptors:
*coronary stent
*artery intima proliferation: DI, diagnosis
*artery intima proliferation: DT, drug therapy
*artery intima proliferation: PC, prevention
*artery intima proliferation: SU, surgery
disease duration
follow up
artery diameter
heart muscle revascularization
restenosis: CO, complication
quantitative diagnosis
human
male
female
major clinical study
human tissue
human cell
aged
adult
article
Drug Descriptors:
*cilostazol: CB, drug combination
*cilostazol: DT, drug therapy
*cilostazol: PD, pharmacology
*ticlopidine: CB, drug combination
*ticlopidine: DT, drug therapy
*ticlopidine: PD, pharmacology

cyclic AMP phosphodiesterase: EC, endogenous compound
cyclic AMP responsive element binding protein: EC, endogenous compound
RN (cilostazol) 73963-72-1; (ticlopidine) 53885-35-1, 55142-85-3; (cyclic AMP phosphodiesterase) **9036-21-9**; (cyclic AMP responsive element binding protein) 130428-87-4, 130939-96-7
NP Palmaz-Schatz stent

L76 ANSWER 47 OF 57 EMBASE

ACCESSION NUMBER: 95339307 EMBASE Full-text
DOCUMENT NUMBER: 1995339307
TITLE: Cyclic nucleotide phosphodiesterases as therapeutic targets in cardiovascular diseases.
AUTHOR: Stoclet J.-C.; Keravis T.; Komas N.; Lugnier C.
CORPORATE SOURCE: Lab. Pharmacol./Physiopathol. Cell., Univ. Louis Pasteur de Strasbourg, Faculte de Pharmacie, CNRS, URA 600, BP 24,F-67401 Illkirch, France
SOURCE: Expert Opinion on Investigational Drugs, (1995) Vol. 4, No. 11, pp. 1081-1100. .
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
025 Hematology
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 1995
Last Updated on STN: 12 Dec 1995

AB Cyclic nucleotide phosphodiesterases (PDEs) comprise at least seven families of isozymes coded by related but distinct genes, grouped on the basis of their structural and enzymatic characteristics. Five of these families are known to be present in the cardiovascular system. A number of potent inhibitors have been synthesised with relative selectivity for some PDEs. However, there is no selective inhibitor of PDE1 (calmodulin-activated), and only one compound has been reported which selectively inhibits PDE2 (stimulated by cGMP). Available information is limited to pharmacological and therapeutic properties of drugs selectively inhibiting two PDEs specific for cAMP (PDE3, inhibited by milrinone-like cardiotonics, and PDE4, inhibited by rolipram) and a cGMP-PDE (PDE5, inhibited by zaprinast). Differential expression of PDEs and differential subcellular localisation provide the possibility of selectively targeting cardiovascular and platelet functions with selective PDE inhibitors. The resulting effects include short- and long-term modulation of cardiac and vascular inotropy, cardiac rhythm and excitability, thrombosis, inflammatory responses to injury and, probably, proliferation of vascular smooth muscle cells. PDE3 inhibitors have been investigated in heart failure. Despite leading to marked haemodynamic improvement, chronic treatment with PDE3 inhibitors does not increase (and may even decrease) survival, due to arrhythmias (probably induced by excessive cAMP accumulation). PDE4 inhibitors are being actively investigated in inflammatory diseases. Their actions in endothelial cells may also lead to antithrombotic effects. PDE5 inhibitors might compensate the pathological impairment of nitric oxide-induced cGMP levels seen in **atherosclerosis** and after endothelial injury. Preclinical studies suggest that they may reduce myointimal proliferation after angioplasty. Identification of isozymes expressed in each tissue and

determination of their possible pathological alterations will probably be possible in the near future. This will afford clarification of the role of PDEs in the cardiovascular system and the potential therapeutic uses of PDE inhibitors.

CT Medical Descriptors:
*cardiovascular disease: DT, drug therapy
animal model
cellular distribution
clinical trial
drug selectivity
drug targeting
gene expression
heart arrhythmia: DT, drug therapy
heart arrhythmia: SI, side effect
heart failure
human
inflammation
nonhuman
review
thrombocyte function
thrombosis
vascular smooth muscle
Drug Descriptors:
*cyclic nucleotide phosphodiesterase: EC, endogenous compound
*isoenzyme: EC, endogenous compound
*phosphodiesterase inhibitor: AE, adverse drug reaction
*phosphodiesterase inhibitor: DV, drug development
*phosphodiesterase inhibitor: CT, clinical trial
*phosphodiesterase inhibitor: DT, drug therapy
*phosphodiesterase inhibitor: PD, pharmacology
amrinone: PD, pharmacology
amrinone: DT, drug therapy
anagrelide: PD, pharmacology
calmodulin: EC, endogenous compound
cilostamide: PD, pharmacology
cyclic amp: EC, endogenous compound
cyclic amp phosphodiesterase: EC, endogenous compound
cyclic gmp: EC, endogenous compound
cyclic gmp phosphodiesterase: EC, endogenous compound
denbufylline: PD, pharmacology
dipyridamole: PD, pharmacology
enoximone: DT, drug therapy
enoximone: PD, pharmacology
enoximone: CT, clinical trial
indolidan: PD, pharmacology
isobutylmethylxanthine: PD, pharmacology
milrinone: DT, drug therapy
milrinone: PD, pharmacology
nimodipine: PD, pharmacology
nitric oxide: EC, endogenous compound
pimobendan: PD, pharmacology
pimobendan: DT, drug therapy
pimobendan: CT, clinical trial
rolipram: PD, pharmacology
saterinone: PD, pharmacology
theophylline: PD, pharmacology
trequinsin: PD, pharmacology
unindexed drug
vinpocetine: PD, pharmacology
zaprinast: PD, pharmacology

zardaverine: PD, pharmacology

RN (cyclic nucleotide phosphodiesterase) 50812-31-2; (amrinone) 60719-84-8; (anagrelide) 68475-42-3; (cilostamide) 68550-75-4; (cyclic amp) 60-92-4; (cyclic amp phosphodiesterase) **9036-21-9**; (cyclic gmp) 7665-99-8; (cyclic gmp phosphodiesterase) 9068-52-4; (denbufylline) 57076-71-8; (dipyridamole) 58-32-2; (enoximone) 77671-31-9; (indolidan) 100643-96-7; (isobutylmethylxanthine) 28822-58-4; (milrinone) 78415-72-2; (nimodipine) 66085-59-4; (nitric oxide) 10102-43-9; (pimobendan) 74150-27-9; (rolipram) 61413-54-5; (saterinone) 102669-89-6; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9; (trequinsin) 78416-81-6; (vinpocetine) 42971-09-5; (zaprinast) 37762-06-4; (zardaverine) 101975-10-4

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ACCESSION NUMBER: 95146708 EMBASE Full-text
DOCUMENT NUMBER: 1995146708
TITLE: Cyclic nucleotide phosphodiesterase inhibitors.
AUTHOR: Demoliou-Mason C.D.
CORPORATE SOURCE: National Heart and Lung Institute, Dovehouse Street,London SW3 6LY, United Kingdom
SOURCE: Expert Opinion on Therapeutic Patents, (1995) Vol. 5, No. 5, pp. 417-430. .
ISSN: 1354-3776 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jun 1995
Last Updated on STN: 12 Jun 1995

AB Cyclic nucleotide phosphodiesterases (PDEs) hydrolyse cyclic nucleotides to their inactive form (5' nucleotides), and thereby play an important role in cellular signalling mechanisms. These enzymes can be classed into seven families (or isozymes/isoenzymes) on the basis of their amino acid sequence, substrate specificity and sensitivity to pharmacological agents. This article reviews each PDE family in turn and analyses the patent literature in each area. Specific attention has been placed on those patents which disclose compounds reported to be useful for the treatment of cardiovascular diseases including thrombosis and **atherosclerosis**.

CT Medical Descriptors:
*patent
*signal transduction
amino acid sequence
atherosclerosis
cardiovascular disease
enzyme specificity
human
nonhuman
review
second messenger
thrombosis
Drug Descriptors:
*cyclic nucleotide: EC, endogenous compound
*cyclic nucleotide phosphodiesterase: EC, endogenous compound
1,4 dihydropyridine derivative: PD, pharmacology
1,4 dihydropyridine derivative: DV, drug development

4 [2 (beta d glucopyranosyloxy) 6 heptyl 4 hydroxybenzoyloxy] 2 heptyl 6 hydroxybenzoic acid
amrinone: PD, pharmacology
benzothiazepine derivative: PD, pharmacology
benzothiazepine derivative: DV, drug development
calcium: EC, endogenous compound
calmodulin: EC, endogenous compound
cyclic amp phosphodiesterase: EC, endogenous compound
cyclic gmp phosphodiesterase: EC, endogenous compound
cyclic nucleotide phosphodiesterase inhibitor: DV, drug development
cyclic nucleotide phosphodiesterase inhibitor: PD, pharmacology
dihydropyridazine derivative: DV, drug development
dihydropyridazine derivative: PD, pharmacology
enoximone: PD, pharmacology
furanone derivative: PD, pharmacology
furanone derivative: DV, drug development
guanine derivative: PD, pharmacology
guanine derivative: DV, drug development
hydroxybenzoic acid derivative: DV, drug development
hydroxybenzoic acid derivative: PD, pharmacology
indazole derivative: DV, drug development
indazole derivative: PD, pharmacology
isoenzyme: EC, endogenous compound
milrinone: PD, pharmacology
piperazine derivative: DV, drug development
piperazine derivative: PD, pharmacology
pyrazolo[4,3 d]pyrimidin 7(6h) one derivative: PD, pharmacology
pyrazolo[4,3 d]pyrimidin 7(6h) one derivative: DV, drug development
pyrazolo[4,3 d]pyrimidine derivative: PD, pharmacology
pyrazolo[4,3 d]pyrimidine derivative: DV, drug development
pyridazine derivative: DV, drug development
pyridazine derivative: PD, pharmacology
quinazoline derivative: DV, drug development
quinazoline derivative: PD, pharmacology
unindexed drug
unclassified drug

RN (cyclic nucleotide phosphodiesterase) 50812-31-2; (amrinone) 60719-84-8; (calcium) 7440-70-2; (cyclic amp phosphodiesterase) **9036-21-9**; (cyclic gmp phosphodiesterase) 9068-52-4; (enoximone) 77671-31-9; (milrinone) 78415-72-2

CO Asahi; Daiichi seiyaku; Pfizer; Sterling winthrop; Ono; Schering; Bristol myers squibb; Asta; Eisai; Syntex; Janssen; Rhone poulenc rorer; Bayer; Celltech; Home products; Smith kline beecham

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ACCESSION NUMBER: 95134959 EMBASE Full-text
DOCUMENT NUMBER: 1995134959
TITLE: Regulatory and catalytic domains of platelet cAMP phosphodiesterases: Targets for drug design.
AUTHOR: Sheth S.B.; Colman R.W.
CORPORATE SOURCE: Sol Sherry Thrombosis Research Ctr., Temple University School of Medicine, 3400 N Broad Street,Philadelphia, PA 19140, United States
SOURCE: Seminars in Hematology, (1995) Vol. 32, No. 2, pp. 110-119.
ISSN: 0037-1963 CODEN: SEHEA3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 025 Hematology

029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 1995
Last Updated on STN: 16 May 1995
CT Medical Descriptors:
*thrombocyte
affinity chromatography
atherosclerosis: DT, drug therapy
atherosclerosis: ET, etiology
blood clot lysis
catalysis
concentration response
drug design
enzyme phosphorylation
graft occlusion
human
nonhuman
priority journal
protein degradation
review
structure activity relation
thrombocyte adhesion
thrombocyte aggregation
thrombosis: DT, drug therapy
Drug Descriptors:
insulin receptor
*adenosine: EC, endogenous compound
*cyclic amp: EC, endogenous compound
*cyclic amp phosphodiesterase: EC, endogenous compound
*guanine nucleotide binding protein: EC, endogenous compound
*plasmin: EC, endogenous compound
*prostacyclin: EC, endogenous compound
*thrombin: EC, endogenous compound
*thromboxane a2: EC, endogenous compound
1,3 dihydro 1,3,3 trimethyl 5 (1,4,5,6 tetrahydro 4 methyl 6 oxo 3 pyridazinyl) 2h indol 2 one
9 (2 hydroxy 3 nonyl)adenine
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
adenosine diphosphate: EC, endogenous compound
adenylate cyclase: EC, endogenous compound
adrenalin: EC, endogenous compound
amrinone
cilostazol: PD, pharmacology
cilostazol: DT, drug therapy
cilostazol: CM, drug comparison
cyclic amp dependent protein kinase: EC, endogenous compound
cyclic amp derivative
cyclic gmp: EC, endogenous compound
dipyridamole: PD, pharmacology
flavonoid
isobutylmethylxanthine
milrinone
phenothiazine derivative
prostaglandin: EC, endogenous compound
rolipram
ticlopidine: DT, drug therapy
ticlopidine: CM, drug comparison

unindexed drug
vinpocetine
zaprinast

RN (adenosine) 58-61-7; (cyclic amp) 60-92-4; (cyclic amp phosphodiesterase) **9036-21-9**; (plasmin) 9001-90-5, 9004-09-5; (prostacyclin) 35121-78-9, 61849-14-7; (thrombin) 9002-04-4; (thromboxane a2) 57576-52-0; (1,3 dihydro 1,3,3 trimethyl 5 (1,4,5,6 tetrahydro 4 methyl 6 oxo 3 pyridazinyl) 2h indol 2 one) 100644-00-6; (9 (2 hydroxy 3 nonyl)adenine) 59262-86-1; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (adenosine diphosphate) 20398-34-9, 58-64-0; (adenylate cyclase) 9012-42-4; (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (amrinone) 60719-84-8; (cilostazol) 73963-72-1; (cyclic gmp) 7665-99-8; (dipyridamole) 58-32-2; (isobutylmethylxanthine) 28822-58-4; (milrinone) 78415-72-2; (rolipram) 61413-54-5; (ticlopidine) 53885-35-1, 55142-85-3; (vinpocetine) 42971-09-5; (zaprinast) 37762-06-4

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ACCESSION NUMBER: 93107199 EMBASE Full-text
DOCUMENT NUMBER: 1993107199
TITLE: Patent Evaluation: Pyrimidinone derivatives as selective cGMP-PDE inhibitors.
SOURCE: Current Opinion in Therapeutic Patents, (1993) Vol. 3, No. 3-4, pp. 475-476. .
ISSN: 0962-2594 CODEN: COTPES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 1993
Last Updated on STN: 16 May 1993

AB Novelty: Novel pyrazolo[4,3-d]pyrimidin-7-ones are claimed to be selective inhibitors of cyclic guanosine 3',5'-monophosphate diesterase (cGMP-PDE). They are potentially useful for the treatment of a variety of cardiovascular disorders including angina, hypertension, heart failure and **atherosclerosis**. Biology: PDE (cGMP and cAMP) inhibitory activity was determined using PDE enzymes isolated from rabbit platelets and rat kidney. IC50 values were in the range 12.0 to 5.5 nM (cGMP). Platelet anti-aggregatory activity and antihypertensive activity are described, but no specific data are provided. Chemistry: A total of forty-four compounds are disclosed and are exemplified by synthesis. Yields, mps and elemental analyses are given. Five compounds are specifically claimed including 5-[2-ethoxy-5-(1-methyl-2-imidazolyl)phenyl]-1-methyl-3-n-propyl-1,6- dihydro-7H -pyrazolo[4,3-d]pyrimidin-7-one.

CT Medical Descriptors:
*enzyme inhibition
angina pectoris
animal cell
animal tissue
antihypertensive activity
atherosclerosis
cardiovascular disease
drug structure
drug synthesis
heart failure
hypertension
kidney
nonhuman

note
rabbit
rat
thrombocyte
Drug Descriptors:
*cyclic gmp phosphodiesterase
*pyrimidinone derivative: DV, drug development
cyclic amp phosphodiesterase
enzyme inhibitor: DV, drug development
thrombocyte aggregation inhibitor: DV, drug development
RN (cyclic gmp phosphodiesterase) 9068-52-4; (cyclic amp phosphodiesterase) **9036-21-9**
CO Pfizer

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ACCESSION NUMBER: 93209045 EMBASE Full-text
DOCUMENT NUMBER: 1993209045
TITLE: Minimally modified low density lipoprotein-induced inflammatory responses in endothelial cells are mediated by cyclic adenosine monophosphate.
AUTHOR: Parhami F.; Fang Z.T.; Fogelman A.M.; Andalibi A.; Territo M.C.; Berliner J.A.
CORPORATE SOURCE: Department of Pathology, UCLA School of Medicine, Center for Health Sciences, 10833 LeConte Avenue,Los Angeles, CA 90024-1732, United States
SOURCE: Journal of Clinical Investigation, (1993) Vol. 92, No. 1, pp. 471-478. .
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 1993
Last Updated on STN: 15 Aug 1993

AB We have previously shown that minimally oxidized LDL (MM-LDL) activated endothelial cells to increase their interaction with monocytes but not neutrophils, inducing monocyte but not neutrophil binding and synthesis of monocyte chemotactic protein-1 and monocyte colony-stimulating factor (M-CSF). In the present studies we have examined the signaling pathways by which this monocyte-specific response is induced. Both induction of monocyte binding and mRNA levels for M-CSF by MM-LDL were not inhibited in protein kinase C-depleted endothelial cells. A number of our studies indicate that cAMP is the second messenger for the effects of MM-LDL cited above. Incubation of endothelial cells with MM-LDL caused a 173% increase in intracellular cAMP levels. Agents which increased cAMP levels, including cholera toxin, pertussis toxin, dibutyryl cAMP, and isoproterenol mimicked the actions of MM-LDL. Agents which elevated cAMP were also shown to activate NFκB, suggesting a role for this transcription factor in activation of monocyte-endothelial interactions. Although endothelial leukocyte adhesion molecule (ELAM) mRNA synthesis can be regulated by NFκB, ELAM was not expressed and ELAM mRNA was only slightly elevated in response to MM-LDL. We present evidence that induction of neutrophil binding by LPS is actually suppressed by agents that elevated cAMP levels.

CT Medical Descriptors:
*endothelium cell
*inflammation: ET, etiology
*monocyte

animal cell
aorta
article
atherosclerosis
binding affinity
binding site
dna probe
electrophoretic mobility
enzyme activity
human
human cell
leukocyte adherence
messenger rna synthesis
microscopy
neutrophil
nonhuman
northern blotting
priority journal
rabbit
Drug Descriptors:
*cholera toxin
*colony stimulating factor 1: EC, endogenous compound
*cyclic amp: EC, endogenous compound
*endothelial leukocyte adhesion molecule 1: EC, endogenous compound
*low density lipoprotein
*messenger rna: EC, endogenous compound
*pertussis toxin
*protein kinase c: EC, endogenous compound
bucladesine
cyclic amp phosphodiesterase: EC, endogenous compound
isoprenaline
RN (colony stimulating factor 1) 81627-83-0; (cyclic amp) 60-92-4; (endothelial leukocyte adhesion molecule 1) 128875-25-2; (pertussis toxin) 70323-44-3; (protein kinase c) 141436-78-4; (bucladesine) 16980-89-5, 362-74-3; (cyclic amp phosphodiesterase) **9036-21-9**; (isoprenaline) 299-95-6, 51-30-9, 6700-39-6, 7683-59-2

L76 ANSWER 52 OF 57 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 79101791 EMBASE Full-text
DOCUMENT NUMBER: 1979101791
TITLE: [Effect of experimental **atherosclerosis** on some metabolic parameters of rabbit aorta. I. Cyclic AMP and phosphodiesterases].
EFFETTO DELL'ATEROSCLEROSI SPERIMENTALE SU ALCUNI PARAMETRI METABOLICI DELL'AORTA DI CONIGLIO. PARTE 1: AMP CICLICO E FOSFODIESTERASI.
AUTHOR: Caparrotta L.; Bonetti A.C.; Carpenedo F.; et al.
CORPORATE SOURCE: Ist. Farmacol., Univ. Padova, Italy
SOURCE: Giornale della Arteriosclerosi, (1978) Vol. 3, No. 2, pp. 131-140. .
CODEN: GIARA5
COUNTRY: Italy
DOCUMENT TYPE: Journal
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: Italian
SUMMARY LANGUAGE: English
CT Medical Descriptors:
***atherosclerosis**
animal experiment

great blood vessel
cytology
Drug Descriptors:
*cyclic amp phosphodiesterase
RN (cyclic amp phosphodiesterase) **9036-21-9**

L76 ANSWER 53 OF 57 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 79030005 EMBASE Full-text
DOCUMENT NUMBER: 1979030005
TITLE: Phthalazinol.
AUTHOR: Castaner J.; Hillier K.
CORPORATE SOURCE: Spain
SOURCE: Drugs of the Future, (1978) Vol. 3, No. 1, pp. 55-58. .
CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
CT Medical Descriptors:
*amyotrophic lateral sclerosis
*artery
***atherosclerosis**
*clinical study
*drug synthesis
*endothelium cell
*enzyme inhibition
*hypertension
*phagocytosis
*rat
*thrombocyte aggregation
animal experiment
therapy
central nervous system
cardiovascular system
heart
oral drug administration
intravenous drug administration
blood and hemopoietic system
Drug Descriptors:
*carbon
*cyclic amp phosphodiesterase
*noradrenalin
*papaverine
*oxagrelate
*pyricarbate
*theophylline
RN (carbon) 7440-44-0; (cyclic amp phosphodiesterase) **9036-21-9**; (noradrenalin) 1407-84-7, 51-41-2; (papaverine) 58-74-2, 61-25-6; (oxagrelate) 56611-65-5; (pyricarbate) 1882-26-4; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9
CO Banyu (Japan)

L76 ANSWER 54 OF 57 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 78232102 EMBASE Full-text
DOCUMENT NUMBER: 1978232102
TITLE: Effects of hydrocortisone on adenylate cyclase and cyclic AMP phosphodiesterase activities and on concentration of cyclic AMP in tissues and body fluids in experimental

atherosclerosis.

AUTHOR: Speranskaya v. N.; Ozerova I.N.; Scherbakova I.A.; Gerasimova E.N.

CORPORATE SOURCE: All-Union Cardiol. Res. Cent., Acad. Med. Sci. USSR, Moscow, Russia

SOURCE: Voprosy Meditsinskoi Khimii, (1977) Vol. 23, No. 6, pp. 777-782. .
CODEN: VMDKAM

COUNTRY: Russia

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index
029 Clinical Biochemistry
003 Endocrinology
020 Gerontology and Geriatrics

LANGUAGE: Russian

SUMMARY LANGUAGE: English

AB Administration of hydrocortisone into healthy rabbits activated adenylate cyclase and phosphodiesterase in liver tissue; activity of the enzymes was normalized within 5 days after the treatment. The hormone, administered into animals with experimental cholesterol-induced **atherosclerosis** , caused an activation of adenylate cyclase and inhibition of phosphodiesterase; due to the phenomenon more distinct and long-term increase in cAMP concentration was observed in kidney, liver and fatty tissues. Concentration of cAMP exceeded considerably its initial content in the tissues within 5 days after the hydrocortisone administration. Hydrocortisone inhibited the adenylate cyclase system activity in adrenal cortex of experimental and control animals at early periods of the experiment. In healthy rabbits content of cAMP was increased in adrenal cortex within 5 days after the hormone administration. As a similar effect was not found in animals with experimental **atherosclerosis** these data suggest that the hypophysis-adrenal cortex system under the experimental conditions studied was inhibited.

CT Medical Descriptors:
*adrenal cortex
***atherosclerosis**
*adipose tissue
*hypophysis
*hypothalamus hypophysis adrenal system
*kidney
*liver
*metabolism
*rabbit
theoretical study
Drug Descriptors:
*adenylate cyclase
*cholesterol
*cyclic amp
*cyclic amp phosphodiesterase
*enzyme
*hydrocortisone
*phosphodiesterase

RN (adenylate cyclase) 9012-42-4; (cholesterol) 57-88-5; (cyclic amp) 60-92-4; (cyclic amp phosphodiesterase) **9036-21-9**; (hydrocortisone) 50-23-7

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ACCESSION NUMBER: 77199162 EMBASE Full-text

DOCUMENT NUMBER: 1977199162

TITLE: Changes of cyclic AMP and cyclic AMP phosphodiesterase in the progression and regression of experimental

atherosclerosis.

AUTHOR: Numano F.; Maezawa H.; Shimamoto T.; Adachi K.
CORPORATE SOURCE: Dept. Int. Med., Tokyo Ika Shika Nat. Univ. Med. Sch., Bunkyo ku, Tokyo, Japan
SOURCE: Annals of the New York Academy of Sciences, (1976) Vol. vol. 275, pp. 311-320. .
CODEN: ANYAA
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English

AB Studies on a therosclerosis have recently been focused on the patophysiologic or metabolic changes of the cellular components of the arterial wall, on their roles in atherogenesis, and on the regression of **atherosclerosis**. Contractive changes of endothelial cells, for instance, have been discussed as an important causative factor of increasing vascular permeability in relation to atherogenesis. There are many studies on the roles of neointimal cells or migrated smooth muscle cells in the progression or regression of **atherosclerosis**. The purpose of this study (using rabbits) was to follow the changes of cyclic nucleotides in the intima, in atheromatous lesions, and in the media of the aortic wall in the progression or regression of **atherosclerosis**, in an attempt to obtain a clue as to what regulates the function of endothelial or neointimal cells in relation to **atherosclerosis**. It appeared that only a few studies exist on the behavior of the cyclic nucleotides during these pathophysiologic conditions of the arterial wall, mainly because the multitude of cells complicates any analysis of the relation between the cAMP levels and the pathologic changes of the arterial cell types. A microassay method made it possible to measure cAMP and cAMP phosphodiesterase (cAMPPDE) in the intima and media. The results show a rather high level of cAMP in the intima compared with that in the media, which suggests susceptibility of the endothelium to the 'external' medium. The assay of cyclic nucleotides also revealed a high activity of cAMPPDE and a low level of cAMP in progressive lesions and, conversely, a decreased activity of cAMPPDE and an increased level of cAMP in regressing lesions. A high activity of cAMPPDE and a low level of cAMP was found in atherosclerotic lesions, characterized by foam cells, fatty degeneration, fibrosis, and scanty smooth muscle cells. These histologic features make one anticipate a decrease in DNA and an increase in cAMP relative to DNA. In the study of the regressive phase, it should be noted that a reverse relation of cAMP and cAMPPDE exists in atheromatous lesions, compared with that in the atherosclerotic lesions of rabbits fed cholesterol for 15 wk. It seems that changes in cyclic nucleotides are a good parameter to evaluate the regressive effect. If one can prevent the increase of cAMPPDE activity and decrease the level of cAMP in atherosclerotic lesions, perhaps **atherosclerosis** may be delayed by modifying the atherosclerotic lesion. From these points of view, it is of interest that in animals treated with EG 626, increased levels of cAMP and a decreased activity of cAMPPDE in the course of regression were found.

CT Medical Descriptors:
*artery wall
***atherosclerosis**
in vitro study
theoretical study
diagnosis
Drug Descriptors:
*cyclic amp
*cyclic amp phosphodiesterase
RN (cyclic amp) 60-92-4; (cyclic amp phosphodiesterase) **9036-21-9**

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ACCESSION NUMBER: 76208296 EMBASE Full-text
DOCUMENT NUMBER: 1976208296
TITLE: Cyclic AMP phosphodiesterase inhibitors in treatment of atherosclerotic diseases and its basic background. Treatment of cerebral **arteriosclerosis** with EG 467; a cyclic AMP phosphodiesterase inhibitor.
AUTHOR: Shimamoto T.; Maezawa H.; Yamazaki H.; et al.
CORPORATE SOURCE: Dept. Med., Tokyo Ika/Shika Nat. Univ., Tokyo, Japan
SOURCE: Japanese Journal of Medicine, (1975) Vol. 14, No. 3, pp. 209-210. .
CODEN: JJMDAT
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
CT Medical Descriptors:
***atherosclerosis**
*brain
*chicken
*enzyme inhibition
*monkey
*rabbit
*rat
in vitro study
theoretical study
Drug Descriptors:
*cyclic amp
*cyclic amp phosphodiesterase
*bucladesine
*phosphodiesterase inhibitor
*very low density lipoprotein
bg 467
oxagrelate
unclassified drug
RN (cyclic amp) 60-92-4; (cyclic amp phosphodiesterase) **9036-21-9**; (bucladesine) 16980-89-5, 362-74-3; (oxagrelate) 56611-65-5
CN Bg 467; Eg 626

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ACCESSION NUMBER: 74213456 EMBASE Full-text
DOCUMENT NUMBER: 1974213456
TITLE: Inhibition of 3',5' cyclic AMP phosphodiesterase by acid mucopolysaccharides and sulfopolysaccharides.
AUTHOR: Stefanovich V.
CORPORATE SOURCE: Pharmaceut. Res. Div., Dept. Biochem., Chem. Werke Albert AG, Wiesbaden, Germany
SOURCE: RES.COMMUN.CHEM.PATH.PHARMACOL., (1974) Vol. 7, No. 3, pp. 557-572. .
CODEN: RCDCBL
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
029 Clinical Biochemistry
LANGUAGE: English
AB Acid mucopolysaccharides of connective tissue and semisynthetic polysaccharides were investigated as inhibitors of bovine heart cyclic 3',5' AMP phosphodiesterase (PDE). Acid mucopolysaccharides inhibited PDE in the following order: heparin > chondroitin sulfate B > chondroitin sulfate A >

chondroitin sulfate C > hyaluronic acid > heparitin sulfate. In the semisynthetic sulfopolysaccharides series with the same or similar sulfate contents the inhibition of PDE is parallel to their increasing molecular weight. The PDE inhibition appears to be dependent not only on the molecular weight but also, when acid mucopolysaccharides are considered, on their sulfate group content. In the series of sulfopolysaccharides examined, sulfoevernan, a new semisynthetic sulfopolyglucan, was the most effective inhibitor of PDE. Sulfoevernan inhibited PDE 71.7% in contrast to heparin which exhibited only 16.6% of PDE inhibition. The ratio of PDE inhibition by sulfoevernan and heparin was similar to their ability to 'release' the 'post heparin' lipase in blood of cholesterol fed rabbits. The following hypothesis is advanced: sulfopolysaccharides inhibit PDE causing an increase in cyclic AMP. Increased cyclic AMP activates 'post heparin' lipase by phosphorylation or by allosteric mechanisms. This inhibition of PDE by sulfopolysaccharides could be a reason for the inhibitory effect of sulfopolysaccharides on the development of **atherosclerosis**.

CT Medical Descriptors:
*2 fluoro 5 nitrophenyl azide
***atherosclerosis**
*blood
*cattle
*connective tissue
*drug comparison
*heart
*rabbit
*sulfopolysaccharide
theoretical study
Drug Descriptors:
*acid glycosaminoglycan
*cholesterol
*chondroitin 4 sulfate
*dermatan sulfate
*chondroitin 6 sulfate
*chondroitin sulfate
*cyclic amp
*cyclic amp phosphodiesterase
*heparin
*hyaluronic acid
*levan
*triacylglycerol lipase
*phosphodiesterase inhibitor

RN (cholesterol) 57-88-5; (chondroitin 4 sulfate) 24967-93-9; (dermatan sulfate) 24967-94-0; (chondroitin 6 sulfate) 25322-46-7; (chondroitin sulfate) 9007-28-7, 9082-07-9; (cyclic amp) 60-92-4; (cyclic amp phosphodiesterase) **9036-21-9**; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (hyaluronic acid) 31799-91-4, 9004-61-9, 9067-32-7; (levan) 50815-13-9, 9013-95-0; (triacylglycerol lipase) 9001-62-1

***** INVENTOR RESULTS *****

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=> d his l55

     (FILE 'HCAPLUS' ENTERED AT 09:21:58 ON 06 JUN 2007)
L55          26 S L54 NOT L43

=> d que l55
L1           73 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "EVERS STEFAN"/AU
L5            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  (773904-83-9/BI OR 773904-84-
                0/BI OR 773904-85-1/BI OR 773904-86-2/BI OR 773904-87-3/BI OR
                773904-88-4/BI OR 773904-89-5/BI OR 9036-21-9/BI)
L6         6777 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L7        25179 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ARTERY, DISEASE"/CT
L8        35151 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ATHEROSCLEROSIS/CT
L9        48956 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ATHEROSCLEROSIS/OBI OR
                ARTERIOSCLEROSIS/OBI
L10        9314 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ARTERIOSCLEROSIS/CT
L11       67514 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L7 OR L8 OR L9 OR L10)
L14        6717 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RESTENOSIS/OBI OR CORONARY
                RESTENOSIS/OBI
L15       68114 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 OR L14
L16         197 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 AND L15
L17     1429462 SEA FILE=HCAPLUS ABB=ON  PLU=ON  1/SX,SC
L18         162 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L17
L22       35469 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG SCREENING/CT
L23       38363 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG/OBI (2A) SCREEN?/OBI
L24       38363 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 OR L23
L25          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 AND L24
L26         104 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PERIPHERAL ARTERIAL OCCLUSIVE
                DISEASE/OBI OR PAOD/OBI
L28             QUE  ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004 OR MY
                <2004 OR REVIEW/DT
L29         120 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 AND L28
L32         113 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 (L) (PAC OR PKT OR DMA OR
                BAC OR THU)/RL
L33       22632 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (INHIBIT?/OBI OR PREVENT?/OBI
                OR TREAT?/OBI) (5A) L15
L34         113 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND L33
L35           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L24 OR L26) AND L34
L36          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 OR L25
L37           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L28
L38         113 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND L28
L39       47885 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RESTENOSIS/OBI OR ATHEROSCLERO
                SIS/OBI
L40          63 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 AND L39
L41        1066 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHODIESTERASE#/OBI (2A)
                (TYPE 4/OBI OR 4/OBI OR D/OBI OR D5/OBI OR D7/OBI)
L42          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 AND L41
L43          26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 OR L37 OR L42
L44          29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("FINGERLE J"/AU OR "FINGERLE
                JUERGEN"/AU OR "FINGERLE JURGEN"/AU)
L45          99 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("GULCHER J"/AU OR  "GULCHER
                JEFFREY"/AU OR "GULCHER JEFFREY R"/AU)
L46          29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HIMBER JACQUES"/AU
L47          23 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("GRETARSDOTTIR S"/AU OR
                "GRETARSDOTTIR SOLVEIG"/AU OR "GRETARSODTTIR S"/AU)
L48         235 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR (L44 OR L45 OR L46 OR
                L47)
L50       18255 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HOFFMAN?/PA,CO,CS
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L51        78933 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ROCHE?/PA,CO,CS
L52        16937 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L50 (L) L51
L53           43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L52 AND L48
L54           27 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L53 AND L28
L55           26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L54 NOT L43


=> d his l74

     (FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 09:39:41 ON 06 JUN 2007)
L74           13 S L64 AND (L71 OR L19 OR L41)

=> d que l74
L1            73 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "EVERS STEFAN"/AU
L19           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PDE4D5/OBI OR PDE4/OBI(W)D5/OB
                 I OR PDE4D7/OBI OR PDE4/OBI(W)D7/OBI
L41         1066 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHODIESTERASE#/OBI (2A)
                 (TYPE 4/OBI OR 4/OBI OR D/OBI OR D5/OBI OR D7/OBI)
L44           29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("FINGERLE J"/AU OR "FINGERLE
                 JUERGEN"/AU OR "FINGERLE JURGEN"/AU)
L45           99 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("GULCHER J"/AU OR  "GULCHER
                 JEFFREY"/AU OR "GULCHER JEFFREY R"/AU)
L46           29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HIMBER JACQUES"/AU
L47           23 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("GRETARSDOTTIR S"/AU OR
                 "GRETARSDOTTIR SOLVEIG"/AU OR "GRETARSODTTIR S"/AU)
L48          235 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR (L44 OR L45 OR L46 OR
                 L47)
L64          568 SEA L48
L71        97463 SEA PHOSPHODIESTERASE#
L74           13 SEA L64 AND (L71 OR L19 OR L41)


=> dup rem l55 l74
FILE 'HCAPLUS' ENTERED AT 09:54:46 ON 06 JUN 2007
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FILE 'DRUGU' ENTERED AT 09:54:46 ON 06 JUN 2007
COPYRIGHT (C) 2007 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L55
PROCESSING COMPLETED FOR L74
L77           35 DUP REM L55 L74 (4 DUPLICATES REMOVED)
                 ANSWERS '1-26' FROM FILE HCAPLUS
                 ANSWERS '27-29' FROM FILE MEDLINE
                 ANSWER '30' FROM FILE BIOSIS
                 ANSWERS '31-34' FROM FILE EMBASE
                 ANSWER '35' FROM FILE DRUGU
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=> d l77 1-26 ibib ab

L77 ANSWER 1 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:545165 HCAPLUS Full-text
DOCUMENT NUMBER: 143:40666
TITLE: Quantitation by serial combinatorial dilution
INVENTOR(S): Berndt, Peter; **Evers, Stefan**; Langen, Hanno
PATENT ASSIGNEE(S): F. **Hoffmann**-La **Roche** A.-G., Switz.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1544620	A1	20050622	EP 2004-29190	20041209 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CA 2490301	A1	20050618	CA 2004-2490301	20041215 <--
CN 1629638	A	20050622	CN 2004-10101309	20041216 <--
US 2005136464	A1	20050623	US 2004-16588	20041217 <--
JP 2005189241	A	20050714	JP 2004-367043	20041220 <--
PRIORITY APPLN. INFO.:			EP 2003-104775 A	20031218 <--

AB The invention provides a method for the quantification of a biomol. in a complex mixture of biomols. which comprises a fractionation of the mixture of biomols. providing at least two fractions with at least one distinct component each. These fractions are then subjected to serial combinatorial dilution Subsequently, the biomol. is detected and identified in the fractions by a method providing a sensitivity threshold and identify information. The quantity of the biomol. is determined by summarizing the number of identifications of the biomol. in each fraction on each dilution level in consideration of the resp. dilution factor. For purpose of normalization this sum may be divided by the total number of identifications of all biomols. in all fractions on all dilution levels.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:463808 HCAPLUS Full-text
DOCUMENT NUMBER: 139:173185
TITLE: Synthesis and Structure-Activity Studies of Novel Orally Active Non-Terpenoic 2,3-Oxidosqualene Cyclase Inhibitors
AUTHOR(S): Dehmlow, Henrietta; Aebi, Johannes D.; Jolidon, Synese; Ji, Yu-Hua; Von Mark, Elisabeth M.; **Himber, Jacques**; Morand, Olivier H.
CORPORATE SOURCE: Pharmaceuticals Division, Preclinical Research, F. **Hoffmann**-La **Roche** Ltd., Basel, CH-4070, Switz.
SOURCE: Journal of Medicinal Chemistry (**2003**), 46(15), 3354-3370
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:173185

AB New orally active non-terpenoic inhibitors of human 2,3-oxidosqualene cyclase (hOSC) are reported. The starting point for the optimization process was a set of compds. derived from a fungicide project, which in addition to showing high affinity for OSC from Candida albicans showed also high affinity for human OSC. Common structural elements of these inhibitors are an amine residue and an electrophilic carbonyl C atom embedded in a benzophenone system, which are at a distance of about 10.7 Å. Considering that the keto moiety is in a potentially labile position, modifications of the substitution pattern at the benzophenone as well as annelated heteroaryl systems were explored. Our approach combined testing of the compds. first for increased binding affinity and for increased stability in vitro. Most promising compds. were then evaluated for their efficacy in lowering plasma total cholesterol (TC) and plasma low-d. lipoprotein cholesterol (LDL-C) in hyperlipidemic hamsters. In this respect, the most promising compds. are the benzophenone derivative 1·fumarate and the benzo[d]isothiazol 24·fumarate, which lowered TC by 40% and 33%, resp.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:418863 HCAPLUS Full-text
TITLE: In situ localization of tissue factor in human thrombi
AUTHOR(S): **Himber, Jacques**; Kling, Dorothee; Fallon, John T.; Nemerson, Yale; Riederer, Markus A.
CORPORATE SOURCE: Pharma Division, Preclinical Research, F. **Hoffmann**-La **Roche** Ltd, Basel, CH-4070, Switz.
SOURCE: Blood (**2002**), 99(11), 4249-4250
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal; Letter
LANGUAGE: English
AB Unavailable
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:227496 HCAPLUS Full-text
DOCUMENT NUMBER: 135:2817
TITLE: Peptide deformylase as an antibacterial drug target: target validation and resistance development
AUTHOR(S): Apfel, Christian M.; Locher, Hans; **Evers, Stefan**; Takacs, Bela; Hubschwerlen, Christian; Pirson, Wolfgang; Page, Malcolm G. P.; Keck, Wolfgang
CORPORATE SOURCE: Pharma Research Basel, F. **Hoffmann**-La **Roche** Ltd., Basel, CH-4070, Switz.
SOURCE: Antimicrobial Agents and Chemotherapy (**2001**), 45(4), 1058-1064
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New inhibitors of peptide deformylase (PDF) which are very potent against the isolated enzyme and show a certain degree of antibacterial activity have recently been synthesized by our group. Several lines of exptl. evidence indicate that these inhibitors indeed interfere with the target enzyme in the bacterial cell. The inhibition of Escherichia coli growth could be counteracted by overexpression of PDF from different organisms, including E. coli, Streptococcus pneumoniae, and Haemophilus influenzae. Conversely, reduced expression of PDF in S. pneumoniae resulted in an increased

susceptibility to the inhibitors. Proteome anal. on two-dimensional gels revealed a shift for many proteins towards lower pI in the presence of PDF inhibitors, as would be expected if the proteins still carry their N-formyl-Met terminus. PDF inhibitors show no antimicrobial activity against E. coli under conditions that make growth independent of formylation and deformylation. The antibacterial activity in E. coli was characterized as bacteriostatic. Furthermore, the development of resistance in E. coli was observed to occur with high frequency (10-7). Resistant mutants show a reduced growth rate, and DNA sequence anal. revealed mutations in their formyl transferase gene. It is concluded that PDF may not be an optimal target for broad-spectrum antibacterial agents.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:227495 HCAPLUS Full-text
DOCUMENT NUMBER: 135:28713
TITLE: Peptide deformylase as an antibacterial drug target: assays for detection of its inhibition in Escherichia coli cell homogenates and intact cells
AUTHOR(S): Apfel, Christian M.; **Evers, Stefan**; Hubschwerlen, Christian; Pirson, Wolfgang; Page, Malcolm G. P.; Keck, Wolfgang
CORPORATE SOURCE: Pharma Research Basel, F. **Hoffmann**-La **Roche** Ltd., Basel, CH-4070, Switz.
SOURCE: Antimicrobial Agents and Chemotherapy (**2001**), 45(4), 1053-1057
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An assay was developed to determine the activity of peptide deformylase (PDF) inhibitors under conditions as close as possible to the physiol. situation. The assay principle is the detection of N-terminal [35S]methionine labeling of a protein that contains no internal methionine. If PDF is active, the deformylation of the methionine renders the peptide a substrate for methionine aminopeptidase, resulting in the removal of the N-terminal methionine label. In the presence of a PDF inhibitor, the deformylation is blocked so that the N-formylated peptide is not processed and the label is detected. Using this assay, it is possible to determine the PDF activity under near-physiol. conditions in a cell-free transcription-translation system as well as in intact bacterial cells.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:361544 HCAPLUS Full-text
DOCUMENT NUMBER: 136:65084
TITLE: Mechanism-related changes in the gene transcription and protein synthesis patterns of Haemophilus influenzae after treatment with transcriptional and translational inhibitors
AUTHOR(S): **Evers, Stefan**; Di Padova, Karin; Meyer, Michelle; Langen, Hanno; Fountoulakis, Michael; Keck, Wolfgang; Gray, Christopher P.
CORPORATE SOURCE: Biological Technologies, F. **Hoffmann**-La **Roche**, Pharmaceutical Research, Basel, CH - 4070, Switz.
SOURCE: Proteomics (**2001**), 1(4), 522-544
Published in: Electrophoresis, 22(7)

CODEN: PROTC7; ISSN: 1615-9853
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB High-resolution two-dimensional gel electrophoresis of pulse-labeled Haemophilus influenzae exts. allows for the separation and quantification of more than five hundred protein spots. We have determined the changes in the protein synthesis patterns triggered by treatment with inhibitors of transcription, Rifampicin (Rif) and translation, Chloramphenicol (Chl), Erythromycin (Ery), Fusidate (Fus), Puromycin (Pur), Kanamycin (Kan), Streptomycin (Str), and Tetracycline (Tet) relative to the total protein synthesis rate. More than 200 spots changed in intensity under at least one condition. With the exception of the aminoglycosides, Kan and Str, all inhibitors triggered a clear increase in the synthesis rates of ribosomal proteins and RNA polymerase subunits. Northern anal. of rpoA, rpoB, rpoC, and six ribosomal protein genes indicated induction of transcription as well as antitermination as part of the mechanism of the regulation of gene expression. Total RNA synthesis was increased after exposure to Chl, Ery, Fus, and Tet, whereas Str had no effect. Rif led to an almost complete shutdown of RNA synthesis. Exposure to Chl, Ery, Fus, Rif, and Tet resulted in a decrease in the concentration of the stringent factor, guanosine 5',3'-bis-diphosphate (ppGpp) whereas Str again had no effect. Thus, as in Escherichia coli, the response of H. influenzae to translational inhibitors appears to be mediated by the regulatory nucleotide ppGpp.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:268239 HCAPLUS Full-text
DOCUMENT NUMBER: 135:86880
TITLE: Inhibition of arterial thrombosis by a soluble tissue factor mutant and active site-blocked factors IXa and Xa in the guinea pig
AUTHOR(S): **Himber, Jacques**; Refino, Canio J.; Burcklen, Louis; Roux, Sebastien; Kirchhofer, Daniel
CORPORATE SOURCE: Preclinical Research Department, F. **Hoffmann** -La **Roche** Ltd., Basel, CH-4070, Switz.
SOURCE: Thrombosis and Haemostasis (**2001**), 85(3), 475-481
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: F. K. Schattauer Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The substrate recognition region of tissue factor contains two residues, Lys165 and Lys166, which are important for macromol. substrate activation by the tissue factor:factor VIIa complex. Replacement of these two residues with alanine in a soluble version of human tissue factor resulted in a mutant, hTFAA, which can bind factor VIIa but forms an enzymically inactive complex. We found that hTFAA inhibits the activity of guinea pig factor VIIa, allowing us to evaluate hTFAA's effects on thrombosis and hemostasis in a guinea pig model of recurrent arterial thrombosis. In addition to heparin, the effects of hTFAA were compared to active site inhibited factor IXa (F.IXai) and factor Xa (F.Xai). We found that hTFAA, F.IXai and F.Xai were potent antithrombotics and may possess a decreased risk of hemorrhage when compared to unfractionated heparin. When administered at a dose that inhibited thrombosis by about 90%, hTFAA neither affected cuticle bleeding nor the activated partial thromboplastin time, and had only a modest effect on the prothrombin time. At equi-efficacious doses, F.IXai, F.Xai and heparin prolonged bleeding times by 20% ($p > 0.5$), 50% ($p < 0.05$) and 100% ($p < 0.01$), resp. In summary, our study demonstrates that, unlike heparin, specific inhibitors of factors VIIa, IXa

and Xa can produce antithrombotic effects without or with only minimally disturbing normal hemostasis. The results further suggest that factor VIIa and factor IXa are especially promising targets for antithrombotic drug development.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:895436 HCAPLUS Full-text
DOCUMENT NUMBER: 134:276908
TITLE: Application of proteome analysis to drug development and toxicology
AUTHOR(S): **Evers, Stefan**; Gray, Christopher P.
CORPORATE SOURCE: PRPI-D, F. **Hoffmann**-La **Roche** Ltd, Basel, CH-4070, Switz.
SOURCE: Proteomics (**2001**), 225-236. Editor(s): Pennington, Stephen R.; Dunn, Michael J. BIOS Scientific Publishers Ltd.: Oxford, UK. CODEN: 69ATBR
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review, with 28 refs., discussing the role of proteome studies in the identification and validation of drug targets, the study of the mechanisms of drug action, and the detection and rationalization of pharmacol. or toxic effects.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:64476 HCAPLUS Full-text
TITLE: Gene expression changes triggered by exposure of Haemophilus influenzae to novobiocin or ciprofloxacin: combined transcription and translation analysis
AUTHOR(S): Gmuender, Hans; Kuratli, Karin; Di Padova, Karin; Gray, Christopher P.; Keck, Wolfgang; **Evers, Stefan**
CORPORATE SOURCE: Pharmaceuticals Division, F. **Hoffmann**-La **Roche** Ltd., Basel, CH-4070, Switz.
SOURCE: Genome Research (**2001**), 11(1), 28-42 CODEN: GEREFS; ISSN: 1088-9051
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal; Letter
LANGUAGE: English
AB The responses of Haemophilus influenzae to DNA gyrase inhibitors were analyzed at the transcriptional and the translational level. High-d. microarrays based on the genomic sequence were used to monitor the expression levels of >80% of the genes in this bacterium. In parallel the proteins were analyzed by two-dimensional electrophoresis. DNA gyrase inhibitors of two different functional classes were used. Novobiocin, as a representative of one class, inhibits the ATPase activity of the enzyme, thereby indirectly changing the degree of DNA supercoiling. Ciprofloxacin, a representative of the second class, obstructs supercoiling by inhibiting the DNA cleavage-resealing reaction. Our results clearly show that different responses can be observed Treatment with the ATPase inhibitor Novobiocin changed the expression rates of many genes, reflecting the fact that the initiation of transcription for many genes is sensitive to DNA supercoiling. Ciprofloxacin mainly stimulated the expression of DNA repair systems as a response to the DNA damage caused by the stable ternary complexes. In addition, changed expression levels were also observed for some genes coding for proteins either annotated as "unknown

function" or "hypothetical" or for proteins not directly involved in DNA topol. or repair.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:185352 HCAPLUS Full-text
TITLE: Effects of GP IIb/IIIa receptor antagonists on the activated clotting time of heparinized blood
AUTHOR(S): **Himber, Jacques**; Burcklen, Louis; Steiner, Beat
CORPORATE SOURCE: Pharma Division, Preclinical Research, F **Hoffmann**-La **Roche** Ltd, Basel, Switz.
SOURCE: Blood (**2000**), 95(6), 2189
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal; Letter
LANGUAGE: English
AB Unavailable
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:125408 HCAPLUS Full-text
DOCUMENT NUMBER: 132:276421
TITLE: Two-dimensional map of the proteome of Haemophilus influenzae
AUTHOR(S): Langen, Hanno; Takacs, Bela; **Evers, Stefan**; Berndt, Peter; Lahm, Hans-Werner; Wipf, Beat; Gray, Christopher; Fountoulakis, Michael
CORPORATE SOURCE: Genomics Technologies, F. **Hoffmann**-La **Roche** Ltd., Pharmaceutical Research, Basel, 4070, Switz.
SOURCE: Electrophoresis (**2000**), 21(2), 411-429
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have constructed a two-dimensional database of the proteome of Haemophilus influenzae, a bacterium of medical interest of which the complete genome, comprising about 1742 open reading frames, has been sequenced. The soluble protein fraction of the microorganism was analyzed by two-dimensional electrophoresis, using immobilized pH gradient strips of various pH regions, gels with different acrylamide concns. and buffers with different trailing ions. In order to visualize low-copy-number gene products, we employed a series of protein extraction and sample application approaches and several chromatog. steps, including heparin chromatog., chromatofocusing and hydrophobic interaction chromatog. We have also analyzed the cell envelope-bound protein fraction using either immobilized pH gradient strips or a two-detergent system with a cationic detergent in the first and an anionic detergent in the second-dimensional separation Different proteins (502) were identified by matrix-assisted laser desorption/ionization mass spectrometry and amino acid composition anal. This is at present one of the largest two-dimensional proteome databases.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:635867 HCAPLUS Full-text
DOCUMENT NUMBER: 130:206

TITLE: Strategies towards a better understanding of antibiotic action. Folate pathway inhibition in Hemophilus influenzae as an example
AUTHOR(S): **Evers, Stefan**; Di Padova, Karin; Meyer, Michelle; Fountoulakis, Michael; Keck, Wolfgang; Gray, Christopher P.
CORPORATE SOURCE: F. **Hoffmann**-La **Roche** Ltd., Basel, CH-4070, Switz.
SOURCE: Electrophoresis (**1998**), 19(11), 1980-1988
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 2-D electrophoresis was applied to the global anal. of the cellular response of H. influenzae to sulfamethoxazole and trimethoprim, both inhibitors of the tetrahydrofolate synthesis. Deregulation of the synthesis rate of 118 proteins, involved in different metabolic pathways, was observed The regulation of the genes involved in the metabolism of the amino acids Met, Thr, Ser, Gly, and Asx was investigated in detail by anal. of protein synthesis and Northern hybridization. The results suggested that the synthesis of Met biosynthetic enzymes in H. influenzae is regulated in a similar fashion as in Escherichia coli. A good correlation between the results obtained by Northern hybridization and quantification of protein synthesis was observed In contrast to trimethoprim, sulfamethoxazole triggered the increased synthesis of the heat shock proteins DnaK, GroEL, and GroES.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:586750 HCAPLUS Full-text
DOCUMENT NUMBER: 129:312992
TITLE: Reference map of the low molecular mass proteins of Haemophilus influenza
AUTHOR(S): Fountoulakis, Michael; Juranville, Jean-Francois; Roeder, Daniel; **Evers, Stefan**; Berndt, Peter; Langen, Hanno
CORPORATE SOURCE: Preclinical Central Nervous System Research Gene Technol., F. **Hoffmann**-La **Roche** Ltd., Basel, CH-4070, Switz.
SOURCE: Electrophoresis (**1998**), 19(10), 1819-1827
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Anal. of the proteome of H. influenzae by 2-D polyacrylamide gel electrophoresis on conventional Tris-glycine gels does not usually result in efficient separation of the proteins in the 5-20 kDa range, which are mainly accumulated in the lower acidic and basic regions. To improve the separation of the low mol. mass proteins, the authors used homogeneous tricine gels of 2 urea concns. in the 2-D separation The tricine gel systems allowed the efficient and reproducible separation of the proteins of the microorganism with masses at 5-20 kDa, however, no proteins with masses <5 kDa were visualized. 80 Proteins migrating in the 5-25 kDa region were identified by matrix assisted laser desorption/ionization-mass spectrometry, of which 40 identified for the first time. The digestion of the low mass proteins often produced only few peptides, which were insufficient for confident identification by mass spectrometry. The identification was occasionally achieved by a sequential digestion with 2 proteases, trypsin, or endoproteinase Lys-C as 1st and carboxypeptidase P as 2nd enzyme. The gel

system described may be useful for the efficient separation of low mol. mass proteins from other organisms to construct standard maps.

L77 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:480840 HCAPLUS Full-text
DOCUMENT NUMBER: 127:108921
TITLE: Preparation of (aminoalkyl)-substituted benzo-heterocyclic compounds with antimycotic and antihypercholesteremic activities
INVENTOR(S): Aebi, Johannes; Lengsfeld, Hans; Dehmlow, Henrietta; Morand, Olivier; **Himber**, **Jacques**; Schmid, Gerard; Maerki, Hans-Peter; Ji, Yu-Hua
PATENT ASSIGNEE(S): F. **Hoffmann**-La **Roche** Ag, Switz.
SOURCE: Eur. Pat. Appl., 40 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 778271	A2	19970611	EP 1996-119172		19961129 <--
EP 778271	A3	20000322			
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
CA 2190708	A1	19970609	CA 1996-2190708		19961119 <--
JP 09176123	A	19970708	JP 1996-326555		19961206 <--
CN 1161328	A	19971008	CN 1996-121501		19961206 <--
CN 1067991	B	20010704			
US 5856503	A	19990105	US 1996-762867		19961206 <--
BR 9605906	A	19980818	BR 1996-5906		19961209 <--
PRIORITY APPLN. INFO.:			CH 1995-3480	A	19951208 <--

OTHER SOURCE(S): MARPAT 127:108921
AB The title compds. [I; dotted line = optional double bond; M = (un)substituted heterocyclic atom grouping; Q = (un)substituted cycloalkyl, (un)substituted alkenyl, (un)substituted alkadienyl, (un)substituted 4-(aminoalkyl)phenyl, etc.; R = (un)substituted aminoalkyl; T = H, alkyl, (un)substituted NH2, CONH2, NO2, CF3, OH], useful as antimycotics and antihypercholesteremics, are prepared and I-containing formulations presented. Thus, allyl[6-[3-(4-bromophenyl)benzo[d]isothiazol-6-yloxy]hexyl]methylamine fumarate, prepared in 4 steps from benzyl mercaptan, demonstrated a IC50 of 3.3 nM for 2,3-oxidosqualene-lanosterol cyclase.

L77 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:476122 HCAPLUS Full-text
DOCUMENT NUMBER: 127:108766
TITLE: Preparation of benzoylphenoxyalkanamines and analogs as anticholesteremics
INVENTOR(S): Aebi, Johannes; Lengsfeld, Hans; Dehmlow, Henrietta; Morand, Olivier; **Himber**, **Jacques**; Schmid, Gerard; Jolidon, Synese; Ji, Yu-Hua
PATENT ASSIGNEE(S): F. **Hoffmann**-La **Roche** Ag, Switz.
SOURCE: Eur. Pat. Appl., 51 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 778264	A1	19970611	EP 1996-118872	19961126 <--
EP 778264	B1	20010711		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2190699	A1	19970609	CA 1996-2190699	19961119 <--
AT 203009	T	20010715	AT 1996-118872	19961126 <--
ES 2161321	T3	20011201	ES 1996-118872	19961126 <--
PT 778264	T	20011228	PT 1996-118872	19961126 <--
BR 9605864	A	19980825	BR 1996-5864	19961205 <--
JP 09221458	A	19970826	JP 1996-326948	19961206 <--
CN 1158844	A	19970910	CN 1996-121502	19961206 <--
US 6034275	A	20000307	US 1996-762827	19961206 <--
US 6441177	B1	20020827	US 1999-464435	19991216 <--
GR 3036869	T3	20020131	GR 2001-401732	20011011 <--
PRIORITY APPLN. INFO.:			CH 1995-3479 A	19951208 <--
			US 1996-762827 A3	19961206 <--

OTHER SOURCE(S): MARPAT 127:108766

AB A1A2NCA3A4LMpTR [I; A1 = alk(en)yl; A2 = (cyclo)alkyl, alkenyl, OH, etc.; A3,A4 = H or alkyl; A1A2,A1A3 = atoms to complete a ring; p = 1 and L = phenylene, alkylene(oxy), alkyleneimino; p = 0 and L = alkenylene, alkadienylene; M = phenylene, pyridinediyl, Z(CH2)q, etc.; R = (un)substituted Ph, etc.; T = CO, CH(OH), C(:NOH), etc.; Z = N-attached piperidinediyl; q = 0 or 1] were prepared as 2,3-oxidosqualene-lanosterol cyclase inhibitors. Thus, 2,5-F2C6H3OMe was acylated by 4-ClC6H4COCl and the deprotected product O-alkenylated by (E)-BrCH2CH:CHCH2Br to give, after amination by CH2:CHCH2NHMe, title compound II. Data for biol. activity of I were given.

L77 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:456762 HCAPLUS Full-text

DOCUMENT NUMBER: 127:187991

TITLE: Two-dimensional map of Haemophilus influenzae following protein enrichment by heparin chromatography

AUTHOR(S): Fountoulakis, Michael; Langen, Hanno; **Evers, Stefan**; Gray, Chris; Takacs, Bela

CORPORATE SOURCE: F. **Hoffmann**-La **Roche** Ltd., Basel, CH-4070, Switz.

SOURCE: Electrophoresis (**1997**), 18(7), 1193-1202
CODEN: ELCTDN; ISSN: 0173-0835

PUBLISHER: Wiley-VCH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two-dimensional gel electrophoresis separates several hundred protein mols. in a single experiment and is efficiently used to study the products expressed by different genomes. Low-copy-number gene products are invisible on a stained 2-dimensional map and must be enriched such that sufficient amts. are present for visualization and identification. The enrichment was investigated of proteins of Haemophilus influenzae by chromatog. on immobilized heparin which has affinity for growth and protein biosynthesis factors. Total soluble proteins of the microorganism were fractionated on Heparin-Actigel which resulted in enrichment of approx. 160 proteins. The eluates, representing about 40% of the applied proteins, were analyzed by 2-dimensional gel electrophoresis and the protein spots were characterized by amino acid composition anal. and matrix-assisted laser desorption ionization mass spectrometry. The proteins enriched by chromatog. on the heparin gel were not exclusively low-copy-number gene products and they did not exclusively belong to one single class of proteins. The proteins that bound to the heparin gel

are indicated in a 2-dimensional protein map which includes >110 newly identified proteins.

L77 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:603034 HCAPLUS Full-text
DOCUMENT NUMBER: 127:257383
TITLE: Dissociation of antithrombotic effect and bleeding time prolongation in rabbits by inhibiting tissue factor function
AUTHOR(S): **Himber, Jacques**; Kirchhofer, Daniel; Riederer, Markus; Tschopp, Thomas B.; Steiner, Beat; Roux, Sebastien P.
CORPORATE SOURCE: Pharma Division, **Hoffmann**-La **Roche** Ltd., Basel, CH-4070, Switz.
SOURCE: Thrombosis and Haemostasis (**1997**), 78(3), 1142-1149
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: Schattauer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antithrombotic and the antihemostatic effects of a monoclonal anti-TF antibody (AP-1) were compared in a model of arterial thrombosis to those of a direct thrombin inhibitor (napsagatran), and heparin. In anesthetized rabbits transient arterial thrombi were induced by mech. damage to the subendothelium of a moderately stenosed carotid artery. Recurrent formation and dislodgement of thrombi resulted in cyclic flow variations (CFVs) which were monitored over 2 h. Rabbits received i.v. either a placebo (control), a monoclonal anti-rabbit TF antibody (AP-1, 0.05 mg/kg as an i.v. bolus repeated every 15 min), a specific low mol. weight thrombin inhibitor (napsagatran, 3 μg/kg/min) or heparin (3 and 13 μg/kg/min). The effect of the inhibitors on the hemostatic system was studied in a sep. set of rabbits by measuring template bleeding times (BT) in the ear arterioles, marginal ear vein, and the nail cuticle of the foreleg. AP-1 and napsagatran showed a similar antithrombotic activity (78 and 80% abolition of the CFVs, resp.), whereas either low or high dose heparin was poorly effective (43 and 40% inhibition of CFVs, resp.). At these antithrombotic doses and even at 4-fold higher dosage, AP-1 did not alter the BT, whereas napsagatran and heparin prolonged the ear vessels and cuticle BT in a dose-dependent manner. Thus, in contrast to direct thrombin inhibition, the blockade of the TF/F.VIIa function did not result in a concomitant prolongation of the bleeding time. Thus, dissociation of antithrombotic and antihemostatic effects indicates that inhibition of the coagulation system at its initial stage represents a promising approach for the development of new anticoagulants.

L77 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:213550 HCAPLUS Full-text
DOCUMENT NUMBER: 126:287791
TITLE: Ro 48-8071, a new 2,3-oxidosqualene:lanosterol cyclase inhibitor lowering plasma cholesterol in hamsters, squirrel monkeys, and minipigs: comparison to simvastatin
AUTHOR(S): Morand, Olivier H.; Aebi, Johannes D.; Dehmlow, Henrietta; Ji, Yu-Hua; Gains, Nigel; Lengsfeld, Hans; **Himber, Jacques**
CORPORATE SOURCE: F. **Hoffmann**-La **Roche** Ltd., Pharmaceuticals Division, Preclinical Cardiovascular Research, Basel, CH-4070, Switz.
SOURCE: Journal of Lipid Research (**1997**), 38(2),

373-390
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 2,3-Oxidosqualene:lanosterol cyclase (OSC, E.C. 5.4.99.7) represents a unique target for a cholesterol lowering drug. Partial inhibition of OSC should reduce synthesis of lanosterol and subsequent sterols, and also stimulate the production of epoxysterols that repress HMG-CoA reductase expression, generating a synergistic, self-limited neg. regulatory loop. Hence, the pharmacol. properties of Ro 48-8071, a new OSC inhibitor, were compared to that of an HMG-CoA reductase inhibitor, simvastatin. Ro 48-8071 blocked human liver OSC and cholesterol synthesis in HepG2 cells in the nanomolar range; in cells it triggered the production of monooxidosqualene, dioxidosqualene, and epoxycholesterol. It was safe in hamsters, squirrel monkeys and Gottingen minipigs at pharmacol. active doses, lowering LDL .apprx.60% in hamsters, and at least 30% in the two other species, being at least as efficacious as safe doses of simvastatin. The latter was hepatotoxic in hamsters at doses >30 μmol/kg/day limiting its window of efficacy. Hepatic monooxidosqualene increased dose-dependently after treatment with Ro 48-8071, up to .apprx.20 μg/g wet liver or less than 1% of hepatic cholesterol, and it was inversely correlated with LDL levels. Ro 48-8071 did not reduce coenzyme Q10 levels in liver and heart of hamsters, and importantly did not trigger an overexpression of hepatic HMG-CoA reductase, squalene synthase, and OSC itself. In strong contrast, simvastatin stimulated these enzymes dramatically, and reduced coenzyme Q10 levels in liver and heart. Altogether these findings clearly differentiate the OSC inhibitor Ro 48-8071 from simvastatin, and support the view that OSC is a distinct key component in the regulation of the cholesterol synthesis pathway.

L77 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:71930 HCAPLUS Full-text
DOCUMENT NUMBER: 126:104363
TITLE: Preparation of sulfate esters of amino sugar derivatives as inhibitors of migration and proliferation of blood vessel smooth muscle cells.
INVENTOR(S): Chucholowski, Alexander; Pech, Michael; **Fingerle, Juergen**; Rouge, Marianne; Iberg, Niggi; Schmid, Gerard; Maerki, Hans Peter; Tschopp, Thomas; Mueller, Rita; Wessel, Hans Peter
PATENT ASSIGNEE(S): F. **Hoffmann**-La **Roche** Ag, Switz.
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 741139	A1	19961106	EP 1996-106537	19960425 <--
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2174582	A1	19961106	CA 1996-2174582	19960419 <--
JP 08301892	A	19961119	JP 1996-101133	19960423 <--
US 5767268	A	19980616	US 1996-639985	19960426 <--
CN 1142501	A	19970212	CN 1996-105841	19960502 <--
CN 1058016	B	20001101		
BR 9602149	A	19980630	BR 1996-2149	19960503 <--
PRIORITY APPLN. INFO.:			CH 1995-1311 A	19950505 <--

OTHER SOURCE(S): MARPAT 126:104363

AB G1NHCOBCONHG2, I, II; [B = alkylene, (substituted) aromatic ring system; G1-G3 = residue of glycopyranoside, glycopyranose, and derivs.; ≥1 of G1-G3 is O-sulfated], were prepared Thus, 2,3,4,5,6-pentaacetyl-D- gluconic acid (benzyl-3,4-di-O-acetyl-2-amino-2,6-didesoxy-α-D- glucopyranosid-6-yl)amide (preparation given) reacted with isophthalic acid to give isophthalic acid bis[[benzyl-3,4-di-O-acetyl-6-(2,3,4,5,6-penta-O- acetyl-D-gluconoylamino)-2,6-didesoxy-α-D-glucopyranosid-2- yl]amide]. This was deacetylated and sulfated to give isophthalic acid bis[[benzyl-2,6-didesoxy-6-(2,3,4,5,6-penta-O-sulfo-D-gluconoylamino)-3,4- di-O-sulfo-α-D-glucopyranosid-2-yl]amide] tetradecylsodium salt. The latter at 1.0 mg/kg i.v. in rats with damaged carotids gave 67% inhibition of neointima formation.

L77 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:69419 HCAPLUS Full-text

DOCUMENT NUMBER: 126:89702

TITLE: Preparation of sulfate esters of aminosugar derivatives for the inhibition of the migration and proliferation of vascular smooth muscle cells.

INVENTOR(S): Chucholowski, Alexander; Pech, Michael; **Fingerle, Juergen**; Rouge, Marianne; Iberg, Niggi; Schmid, Gerard; Maerki, Hans Peter; Tschopp, Thomas; Mueller, Rita; Wessel, Hans Peter

PATENT ASSIGNEE(S): F. **Hoffmann**-La **Roche** Ag, Switz.

SOURCE: Eur. Pat. Appl., 59 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 741128	A2	19961106	EP 1996-106471	19960424 <--
EP 741128	A3	19970326		
EP 741128	B1	20010620		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2174583	A1	19961106	CA 1996-2174583	19960419 <--
JP 08301839	A	19961119	JP 1996-100874	19960423 <--
JP 2881752	B2	19990412		
AT 202339	T	20010715	AT 1996-106471	19960424 <--
ES 2160190	T3	20011101	ES 1996-106471	19960424 <--
PT 741128	T	20011130	PT 1996-106471	19960424 <--
US 5830920	A	19981103	US 1996-639986	19960426 <--
CN 1150589	A	19970528	CN 1996-100231	19960430 <--
BR 9602148	A	20050621	BR 1996-2148	19960503 <--
GR 3036660	T3	20011231	GR 2001-401520	20010918 <--

PRIORITY APPLN. INFO.: CH 1995-1310 A 19950505 <--

AB (A1X1)m1(Y1X2)n1(Q1X3)m2(Y2X4)n2(Z1X5)m3(Y3X6)n3D(Y6X12)n6(Z2X11)m6(Y5X10)n5(Q2X9)m5(Y4X8)n4(A2X7)m4, (A1X1)m1(Y1X2)n1(Q1X3)m2(Y2X4)n2(Z1X5)m3(Y3X6)n3W[(Y9X18)n9(Z3X17)m9(Y8X16)n8(Q3X15)m8(Y7X14)n7(A3X13)m7][(Y6X12)n6(Z2X11)m6(Y5X10)n5(Q2X9)m5(Y4X8)n4(A2X7)m4] n1-n9, m1-m9 = 0, 1; X1-X18 = O, CONR1, NR1; [R1 = H, alkyl; W = Ph or s-triazine residue; A1-A3 = sugar or sugar acid residue, tris(hydroxymethyl)methyl residue; Y1-Y9 = aromatic ring systems; D = divalent sugar or sugar acid residue; Q1-Q3, Z1-Z3 = D, didesoxyglucopyranoside residue; ≥1 of A1-A3, D, Q1-Q3, Z1-Z3 is sulfated], were prepared Thus, 2,3:4,5-di-O-isopropylidene-1,6-bis-O-(4-methylphenylsulfonyl)galactitol, Me (E)-3-(4-hydroxyphenyl)acrylate, and K2CO3

were stirred 18 h at 130° to give 2,3:4,5-di-O-isopropylidene- 1,6-bis-O-[(E)-4-(2-methoxycarbonylvinyl)phenyl]galactitol, which was converted to 1,6-bis-O-[4-[2-(2,3,4,5,6-penta-O-sulfo-D-glucit-1- ylcarbamoyl)ethyl]phenyl]-2,3,4,5-tetra-O-sulfogalactitol tetradecylsodium salt. The latter at 3 mg/kg/h i.v. in rats with damaged left carotids gave 47% inhibition of tissue proliferation.

L77 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:969418 HCAPLUS Full-text
DOCUMENT NUMBER: 124:202946
TITLE: Preparation of sulfate esters of sugar alcohols for the treatment of arteriosclerotic changes in the vascular walls.
INVENTOR(S): Chucholowski, Alexander; **Fingerle**, **Juergen**; Iberg, Niggi; Maerki, Hans Peter; Mueller, Rita; Pech, Michael; Rouge, Marianne; Schmid, Gerard; Tschopp, Thomas; Wessel, Hans Peter
PATENT ASSIGNEE(S): F. **Hoffmann**-La **Roche** AG, Switz.
SOURCE: Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 663391	A1	19950719	EP 1995-100180	19950109 <--
EP 663391	B1	19970409		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5521160	A	19960528	US 1995-368519	19950104 <--
CA 2139720	A1	19950715	CA 1995-2139720	19950106 <--
ZA 9500086	A	19950720	ZA 1995-86	19950106 <--
AU 9510106	A	19950727	AU 1995-10106	19950109 <--
AU 685196	B2	19980115		
HU 72412	A2	19960429	HU 1995-52	19950109 <--
AT 151416	T	19970415	AT 1995-100180	19950109 <--
ES 2101583	T3	19970701	ES 1995-100180	19950109 <--
IL 112284	A	19981030	IL 1995-112284	19950109 <--
FI 9500127	A	19950715	FI 1995-127	19950111 <--
CN 1109889	A	19951011	CN 1995-101166	19950111 <--
CN 1043349	B	19990512		
RU 2139854	C1	19991020	RU 1995-100773	19950111 <--
NO 9500137	A	19950717	NO 1995-137	19950113 <--
JP 07206803	A	19950808	JP 1995-3729	19950113 <--
JP 2862489	B2	19990303		
PL 180273	B1	20010131	PL 1995-306797	19950113 <--
BR 9500096	A	19951031	BR 1995-96	19951013 <--
PRIORITY APPLN. INFO.:			CH 1994-114 A	19940114 <--
			CH 1994-3315 A	19941107 <--

OTHER SOURCE(S): CASREACT 124:202946; MARPAT 124:202946
AB AX(CH2)mB(CH2)pXA [A = sugar alc. residue (derivative), tris(hydroxymethyl)methyl; ≥1 of the A OH groups are esterified with H2SO4; jX = NR1CO, NHCONH, NHCSNH, NHSO2, NR1, O; m, p = 0, 1; R1 = H, alkyl, hydroxyalkyl; B = system of conjugated multiple bonds], were prepared Thus, (Z)-3-[3-biphenyl-4-yloxymethyl-5-[(Z)-3-carboxyacryloylamino]phenylcarbamoyl]acrylic acid in DMF was treated successively with 4-methylmorpholine, 2-chloro-4,6-dimethoxy-1,3,5- triazine, and D-glucamine to give (Z)-butenedioic acid (Z)-[3-biphenyl-4-yloxymethyl-5-

(3-D-glucit-1- ylcarbamoylacryloylamino)phenylamide]-D-glucit-1-ylamide, which was converted to (Z)-butenedioic acid (Z)-[3-biphenyl-4-yloxymethyl-5-[3-(2,3,4,5,6-penta-O-sulfo-D-glucit-1-ylcarbamoyl)acryloylamino]phenylamide]-(2,3,4,5,6-penta-O-sulfo-D-glucit-1-yl)amide. The latter had 2.2 times the antiproliferative activity of heparin without showing appreciable anticoagulative activity.

L77 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:17444 HCAPLUS Full-text
DOCUMENT NUMBER: 124:106080
TITLE: Mechanism of inhibition of neointimal formation by the angiotensin-converting enzyme inhibitor cilazapril: a study in balloon catheter-injured rat carotid arteries
AUTHOR(S): **Fingerle, Jurgen**; Muller, Rita M. K.; Kuhn, Herbert; Pech, Michael; Baumgartner, Hans Rudolf
CORPORATE SOURCE: Preclin. Research, Pharma Div., F. **Hoffmann** -La **Roche** Ltd, Basel, Switz.
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (**1995**), 15(11), 1945-50
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of cilazapril were studied on all phases of the response to the title injury, i.e., on proliferation of smooth muscle cells (SMCs) in the media, their migration, their proliferation in the neointima, and their deposition of extracellular matrix in the neointima. Although treatment was discontinued after 2 wk, the inhibitory effect of cilazapril on neointimal formation was evident even 52 wk after injury. The amount of extracellular matrix deposited in the intima during cilazapril treatment was decreased by 20% 2 wk after injury, but no effect was seen when the tissues were analyzed after 4 or 52 wk. [3H]Thymidine-labeled cells showed a 50% decrease of SMC labeling in the tunica media, but no inhibition of labeling was seen in the neointima. The fraction of unlabeled neointimal cells in the cilazapril-treated rats, as judged from continuous labeling expts., was decreased by 86%. These data suggest an antiproliferative effect of cilazapril on medial SMCs and an inhibition of SMC migration into the intima. Since intimal extracellular matrix deposition was only delayed, and not blocked, the decrease in medial SMC proliferation and subsequent migration seems to be the main reason for the reduction of neointima formation.

L77 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:740377 HCAPLUS Full-text
DOCUMENT NUMBER: 123:188081
TITLE: Effects of stigmastanyl-phosphocholine (Ro 16-6532) and lovastatin on lipid and lipoprotein levels and lipoprotein metabolism in the hamster on different diets
AUTHOR(S): **Himber, Jacques**; Missano, Brigitte; Rudling, Mats; Hennes, Ulrike; Kempen, Herman J.
CORPORATE SOURCE: F. **Hoffmann**-La **Roche** AG, Pharma Preclin. Res., Basel, CH-4002, Switz.
SOURCE: Journal of Lipid Research (**1995**), 36(7), 1567-85
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies from the laboratory have shown that oral administration of stigmastanyl-phosphocholine (Ro 16-6532) reduces plasma cholesterol levels in exptl. animals on diets free of added cholesterol. In the present study, effects of Ro 16-6532 and lovastatin on lipoprotein levels and metabolism were investigated in male golden Syrian hamsters. In hamsters fed a standard diet, Ro 16-6532 (1 mmol/kg/day) lowered cholesterol in all lipoprotein fractions, as well as apoB-100 and apoA-I. In contrast, lovastatin (25 μmol/kg/day) lowered high d. lipoprotein (HDL)-cholesterol but had no effect on low d. lipoprotein (LDL)-cholesterol or on apoB-100 or apoA-I while triglycerides and very low d. lipoprotein (VLDL)-cholesterol increased. In hamsters fed a coconut fat-supplemented diet, Ro 16-6532 reduced all lipoproteins, with a stronger effect on VLDL- and LDL- than on HDL-cholesterol. Also apoB-100 was reduced. Lovastatin (50 μmol/kg/day) reduced LDL-cholesterol, HDL-cholesterol, and apoA-I while triglycerides and VLDL-cholesterol increased. The drop in LDL-cholesterol seen with both drugs in hamsters fed the diet supplemented with coconut fat occurred without any effect on the plasma removal rate of homologous LDL, or on the content of hepatic LDL-receptors. In contrast, the first phase of removal of homologous radioiodinated VLDL from plasma was markedly increased by both compds., paralleled with an increased uptake of label in the liver and a decreased appearance of labeled apoB-100 in the LDL-fraction. Furthermore, retinyl ester-labeled chylomicrons were also cleared more rapidly in hamsters treated with Ro 16-6532. Hepatic uptake of label from VLDL and chylomicrons was strongly decreased by pre-injection of lactoferrin. In addition, Ro 16-6532 slightly decreased the secretion rate of VLDL in hamsters fed the coconut fat-supplemented diet. Taken together, these results indicate that the reduction of LDL-cholesterol after treatment with Ro 16-6532 and lovastatin observed in the hamster is mainly due to decreased conversion of VLDL into LDL, consequent to an increased hepatic removal of VLDL remnants. Ro 16532 also increased the liver uptake of chylomicron remnants. The hepatic uptake system implicated in the remnant removal can be completely blocked by lactoferrin. The nature of this uptake system is still unknown.

L77 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:954150 HCAPLUS Full-text
DOCUMENT NUMBER: 123:337421
TITLE: Mononuclear leukocytes invade rabbit arterial intima during thickening formation via CD18- and VLA-4-dependent mechanisms and stimulate smooth muscle migration
AUTHOR(S): Kling, Dorothee; **Fingerle, Juergen**; Harlan, John M.; Lobb, Roy R.; Lang, Florian
CORPORATE SOURCE: Preclinical Research, **Hoffmann**-La **Roche** Ltd., Basel, Switz.
SOURCE: Circulation Research (**1995**), 77(6), 1121-8
CODEN: CIRUAL; ISSN: 0009-7330
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of mononuclear leukocytes for the migration of smooth muscle cells (SMCs) during intimal thickening was investigated in the rabbit model of elec. stimulated carotid artery. The approach was to inhibit leukocyte entry into the arterial intima with antibodies against the adhesion mols. very late activation antigen-4 (VLA-4) and CD11/CD18. In elec. stimulated control rabbits treated either with saline or a nonspecific antibody, all types of granulocytes, monocytes, and lymphocytes migrated across and intact endothelium into the acellular subendothelial space, followed by the movement of SMCs from the media into the intima within 36 h of applying elec. current. Treatment of the rabbits with monoclonal antibody (mAb) HP1/2 directed toward

the α4 subunit (CD49d) of VLA-4 inhibited mononuclear leukocyte invasion (consisting of monocytes and lymphocytes) by ≈70% compared with the IgG-treated control rabbits and completely abolished the minimal influx of basophils and eosinophils after 36 h. Neutrophil infiltration, however, remained unaffected by anti-VLA-α4 treatment. Under these conditions, SMC migration across the internal elastic lamina was reduced by 50%. The use of mAb HP1/2 together with mAb 60.3 (directed to the β2 chain of CD11/CD18) completely abolished the influx of monocytes, lymphocytes, and all types of granulocytes into the arterial intima. This complete blockade of leukocyte infiltration resulted in a 70% reduction of intimal SMC accumulation. Together with the previous findings excluding neutrophils as stimulators of SMC migration, the present results indicate that mononuclear leukocytes promote lesion development by stimulating SMC migration.

L77 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:236411 HCAPLUS Full-text
DOCUMENT NUMBER: 120:236411
TITLE: Lack of effect on the low density lipoprotein receptor in hamsters treated with 17α-ethynylestradiol
AUTHOR(S): **Himber, Jacques**; Missano, Brigitte; Kuhl, Herbert
CORPORATE SOURCE: Pharma Division, Preclinical Research, Department of Cardiovascular Diseases, F. **Hoffmann**-La **Roche** Ltd., Basel, CH-4002, Switz.
SOURCE: Biochimica et Biophysica Acta, Lipids and Lipid Metabolism (**1994**), 1211(3), 359-63
CODEN: BBLLA6; ISSN: 0005-2760
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB High pharmacol. doses of 17α-ethynylestradiol are known to increase the number of low d. lipoproteins (LDL)-receptors in rats and rabbits, leading to a profound decrease in plasma cholesterol levels. Here, using rats as a pos. control, the authors demonstrate that in hamsters ethynylestradiol does not upregulate liver LDL-receptors, nor change plasma LDL turnover or plasma LDL-cholesterol. The lack of effect in estradiol-treated hamsters suggests that the hormonal control is different from that in rats.

L77 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:598986 HCAPLUS Full-text
DOCUMENT NUMBER: 119:198986
TITLE: Horizontal semi-dry electroblotting for the detection of the low density lipoprotein receptor in solubilized liver membranes
AUTHOR(S): **Himber, Jacques**
CORPORATE SOURCE: Pharma Div., E. **Hoffmann**-La **Roche** Ltd., Basel, CH-4002, Switz.
SOURCE: Electrophoresis (**1993**), 14(8), 794-7
CODEN: ELCTDN; ISSN: 0173-0835
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A high efficiency transfer of the low d. lipoprotein (LDL) receptor proteins from polyacrylamide slab gel onto immobilizing nitrocellulose membranes using the horizontal semi-dry electrophoretic system is described. The transfer of the LDL receptors from solubilized rat liver microsomes was performed between two graphite plate electrodes in a continuous buffer system containing methanol and sodium dodecyl sulfate. The protein transfer was achieved in

only 150 min at a constant current of 0.8 mA/cm2 at room temperature with very low Joule heat development. The homogeneous elec. field yield between the two electrode plates produced a satisfactory transfer of the LDL-receptor protein band in spite of its high mol. weight, and only few protein traces remained in the polyacrylamide gel after blotting. This improved method allows a rapid and quant. transfer of the LDL receptors without protein denaturation, since the specific binding activity of the blotted receptor is retained as demonstrated by ligand-blotting and immunoblotting.

=> d l77 27-35 ibib ab

L77 ANSWER 27 OF 35 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005245362 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15882609
TITLE: Genes contributing to risk for common forms of stroke.
AUTHOR: **Gulcher Jeffrey R; Gretarsdottir Solveig** ; Helgadottir Anna; Stefansson Kari
CORPORATE SOURCE: deCODE genetics, Sturlagata 8, Reykjavik, Iceland 101.
SOURCE: Trends in molecular medicine, (2005 May) Vol. 11, No. 5, pp. 217-24. Ref: 64
Journal code: 100966035. ISSN: 1471-4914.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 11 May 2005
Last Updated on STN: 19 Aug 2005
Entered Medline: 18 Aug 2005

AB The quest for disease genes that confer risk for stroke is now being undertaken using three complementary approaches. Positional cloning using rare Mendelian phenocopies of stroke has found genes that contribute to rare forms of stroke but, so far, not to the common forms of stroke. Candidate-gene case-control association studies using the common forms of stroke have found suggestive associations of modest effect. However, positional cloning using hundreds of Icelandic families affected by the common forms of stroke has recently found two genes conferring substantial risk for ischemic stroke that have apparently been confirmed in the USA and other European populations. Both genes encode enzymes, **phosphodiesterase** 4D (PDE4D) and arachidonate 5-lipoxygenase- activating protein (FLAP), which suggest novel treatment strategies for stroke prevention.

L77 ANSWER 28 OF 35 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003456109 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14517540
TITLE: The gene encoding **phosphodiesterase** 4D confers risk of ischemic stroke.
AUTHOR: **Gretarsdottir Solveig**; Thorleifsson Gudmar; Reynisdottir Sigridur Th; Manolescu Andrei; Jonsdottir Sif; Jonsdottir Thorbjorg; Gudmundsdottir Thorunn; Bjarnadottir Sigrun M; Einarsson Olafur B; Gudjonsdottir Herdis M; Hawkins Malcolm; Gudmundsson Gudmundur; Gudmundsdottir Hrefna; Andrason Hjalti; Gudmundsdottir Asta S; Sigurdardottir Matthildur; Chou Thomas T; Nahmias Joseph; Goss Shyamali; Sveinbjornsdottir Sigurlaug; Valdimarsson

Einar M; Jakobsson Finnbogi; Agnarsson Uggi; Gudnason Vilmundur; Thorgeirsson Gudmundur; **Fingerle Jurgen** ; Gurney Mark; Gudbjartsson Daniel; Frigge Michael L; Kong Augustine; Stefansson Kari; **Gulcher Jeffrey R**

CORPORATE SOURCE: deCODE Genetics, Sturlugata 8, IS-101 Reykjavik, Iceland.. solveig.gretarsdottir@decode.is

SOURCE: Nature genetics, (2003 Oct) Vol. 35, No. 2, pp. 131-8. Electronic Publication: 2003-09-21. Journal code: 9216904. ISSN: 1061-4036.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-AY245866; GENBANK-AY245867

ENTRY MONTH: 200312

ENTRY DATE: Entered STN: 1 Oct 2003
Last Updated on STN: 18 Dec 2003
Entered Medline: 8 Dec 2003

AB We previously mapped susceptibility to stroke to chromosome 5q12. Here we finely mapped this locus and tested it for association with stroke. We found the strongest association in the gene encoding **phosphodiesterase** 4D (PDE4D), especially for carotid and cardiogenic stroke, the forms of stroke related to atherosclerosis. Notably, we found that haplotypes can be classified into three distinct groups: wild-type, at-risk and protective. We also observed a substantial disregulation of multiple PDE4D isoforms in affected individuals. We propose that PDE4D is involved in the pathogenesis of stroke, possibly through atherosclerosis, which is the primary pathological process underlying ischemic stroke.

L77 ANSWER 29 OF 35 MEDLINE on STN

ACCESSION NUMBER: 2005454177 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 16120840

TITLE: Comment on the **phosphodiesterase** 4D replication study by Bevan et al.

AUTHOR: **Gretarsdottir Solveig; Gulcher Jeffrey;** Thorleifsson Gudmar; Kong Augustine; Stefansson Kari

SOURCE: Stroke; a journal of cerebral circulation, (2005 Sep) Vol. 36, No. 9, pp. 1824. Journal code: 0235266. E-ISSN: 1524-4628.

PUB. COUNTRY: United States

DOCUMENT TYPE: Commentary
Letter

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200601

ENTRY DATE: Entered STN: 26 Aug 2005
Last Updated on STN: 13 Jan 2006
Entered Medline: 12 Jan 2006

L77 ANSWER 30 OF 35 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:262837 BIOSIS Full-text

DOCUMENT NUMBER: PREV200510048748

TITLE: The gene encoding **phosphodiesterase** 4D confers risk of ischemic stroke (vol 35, pg 131, 2003).

AUTHOR(S): **Gretarsdottir, S.**; Thorleifsson, G.; Reynisdottir, S. Th; Manolescu, A.; Jonsdottir, S.; Jonsdottir, T .; Gudmundsdottir, T.; Bjarnadottir, S. M.; Einarsson, O. B.; Gudjonsdottir, H. M.; Hawkins, M.;

Gudmundsson, G.; Gudmundsdottir, H.; Andrason, H.; Gudmundsdottir, A. S.; Sigurdardottir, M.; Chou, T. T.; Nahmias, J.; Goss, S.; Sveinbjornsdottir, S.; Valdimarsson, E. M.; Jakobsson, F.; Agnarsson, U.; Gudnason, V.; Thorgeirsson, G.; **Fingerle, J.**; Gurney, M.; Gudbjartsson, D.; Frigge, M. L.; Kong, A.; Stefansson, K.; Gulcher, J. R.

SOURCE: Nature Genetics, (MAY 2005) Vol. 37, No. 5, pp. 555. ISSN: 1061-4036.
DOCUMENT TYPE: Article
Errata
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jul 2005
Last Updated on STN: 14 Jul 2005

L77 ANSWER 31 OF 35 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006477892 EMBASE Full-text
TITLE: Reply to Many hypotheses but no replication for the association between PDE4D and stroke [2].
AUTHOR: Gulcher J.R.; Kong A.; **Gretarsdottir S.**; Thorleifsson G.; Stefansson K.
CORPORATE SOURCE: J.R. Gulcher, DeCODE Genetics, Sturlugata 8, 101 Reykjavik, Iceland. jeffrey.gulcher@decode.is
SOURCE: Nature Genetics, (2006) Vol. 38, No. 10, pp. 1092-1093. .
Refs: 10
ISSN: 1061-4036 E-ISSN: 1546-1718 CODEN: NGENEC
PUBLISHER IDENT.: NG10061092
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Oct 2006
Last Updated on STN: 16 Oct 2006

L77 ANSWER 32 OF 35 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005406867 EMBASE Full-text
TITLE: Comment on the **Phosphodiesterase** 4D replication study by Bevan et al [4].
AUTHOR: **Gretarsdottir S.; Gulcher J.**; Thorleifsson G.; Kong A.; Stefansson K.
CORPORATE SOURCE: Dr. S. Gretarsdottir, DeCODE Genetics, Reykjavik, Iceland
SOURCE: Stroke, (2005) Vol. 36, No. 9, pp. 1824. .
Refs: 2
ISSN: 0039-2499 CODEN: SJCCA7
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 008 Neurology and Neurosurgery
017 Public Health, Social Medicine and Epidemiology
022 Human Genetics
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Oct 2005
Last Updated on STN: 6 Oct 2005

L77 ANSWER 33 OF 35 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights

reserved on STN
ACCESSION NUMBER: 2005207376 EMBASE Full-text
TITLE: Erratum: The gene encoding **phosphodiesterase** 4D confers risk of ischemic stroke (Nature Genetics (2003) 35 (131-138)).
AUTHOR: **Gretarsdottir S.**; Thorleifsson G.; Reynisdottir S.Th.; Manolescu A.; Jonsdottir S.; Jonsdottir T.; Gudmundsdottir T.; Bjarnadottir S.M.; Einarsson O.B.; Gudjonsdottir H.M.; Hawkins M.; Gudmundsson G.; Gudmundsdottir H.; Andrason H.; Gudmundsdottir A.S.; Sigurdardottir M.; Chou T.T.; Nahmias J.; Goss S.; Sveinbjornsdottir S.; Valdimarsson E.M.; Jakobsson F.; Agnarsson U.; Gudnason V.; Thorgeirsson G.; **Fingerle J.**; Gurney M.; Gudbjartsson D.; Frigge M.L.; Kong A.; Stefansson K.; Gulcher J.R.
SOURCE: Nature Genetics, (2005) Vol. 37, No. 5, pp. 555. .
ISSN: 1061-4036 CODEN: NGENEC
COUNTRY: United States
DOCUMENT TYPE: Journal; Errata
FILE SEGMENT: 022 Human Genetics
LANGUAGE: English
ENTRY DATE: Entered STN: 26 May 2005
Last Updated on STN: 26 May 2005

L77 ANSWER 34 OF 35 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004020579 EMBASE Full-text
TITLE: A call for accurate phenotype definition in the study of complex disorders (multiple letters).
AUTHOR: Funalot B.; Varenne O.; Mas J.-L.; Gulcher J.R.; **Gretarsdottir S.**; Kong A.; Stefansson K.
CORPORATE SOURCE: B. Funalot, Department of Neurology, Hopital Sainte-Anne, 1 rue Cabanis, 75014 Paris, France.
benoit.funalot@broca.inserm.fr
SOURCE: Nature Genetics, (2004) Vol. 36, No. 1, pp. 3-4. .
ISSN: 1061-4036 CODEN: NGENEC
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 008 Neurology and Neurosurgery
018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004

L77 ANSWER 35 OF 35 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1992-02813 DRUGU P Full-text
TITLE: Dipyridamole Inhibits Neointima-Formation in the Rabbit Carotid Artery After Ballooning.
AUTHOR: **Fingerle J**; Noll B; Eisert W G; Brickl R; Mueller T H
CORPORATE SOURCE: Thomae
LOCATION: Tubingen, Biberach, Germany,West
SOURCE: Thromb.Haemostasis (65, No. 6, 1253, 1991) 2 Ref.
CODEN: THHADQ ISSN: 0340-6245
AVAIL. OF DOC.: Department of Physiology 1, University, Tuebingen, Germany.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB Dipyridamole has been reported to inhibit intimal smooth muscle cell proliferation in rabbits after repeated injury of the ear artery with skin forceps. In the present study, p.o. dipyridamole, at therapeutic plasma levels, also strongly reduced neointima formation 2 wk after ballooning of the carotid artery. The agent may be beneficial for the prevention of restenosis after angioplasty in man. (congress abstract).

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=> d his nofile

     (FILE 'HOME' ENTERED AT 08:45:50 ON 06 JUN 2007)

     FILE 'HCAPLUS' ENTERED AT 08:46:20 ON 06 JUN 2007
                E US2005-552181/APPS
                E US2006-552181/APPS
                E EVERS S/AU
                E EVERS STEFAN/AU
L1            73 SEA ABB=ON  PLU=ON  "EVERS STEFAN"/AU
L2            27 SEA ABB=ON  PLU=ON  L1 AND P/DT
L3            96 SEA ABB=ON  PLU=ON  PDE4D/OBI
L4             1 SEA ABB=ON  PLU=ON  L2 AND L3
                D ALL
                SEL RN

     FILE 'REGISTRY' ENTERED AT 08:49:33 ON 06 JUN 2007
L5             8 SEA ABB=ON  PLU=ON  (773904-83-9/BI OR 773904-84-0/BI OR
                773904-85-1/BI OR 773904-86-2/BI OR 773904-87-3/BI OR 773904-88
                -4/BI OR 773904-89-5/BI OR 9036-21-9/BI)

     FILE 'HCAPLUS' ENTERED AT 08:49:54 ON 06 JUN 2007
L6          6777 SEA ABB=ON  PLU=ON  L5
                E ARTERY, DISEASE/CT
L7         25179 SEA ABB=ON  PLU=ON  "ARTERY, DISEASE"/CT
L8         35151 SEA ABB=ON  PLU=ON  ATHEROSCLEROSIS/CT
L9         48956 SEA ABB=ON  PLU=ON  ATHEROSCLEROSIS/OBI OR ARTERIOSCLEROSIS/OBI

L10         9314 SEA ABB=ON  PLU=ON  ARTERIOSCLEROSIS/CT
L11        67514 SEA ABB=ON  PLU=ON  (L7 OR L8 OR L9 OR L10)
L12          195 SEA ABB=ON  PLU=ON  L6 AND L11
L13            0 SEA ABB=ON  PLU=ON  RESTENOSIS/CT
L14         6717 SEA ABB=ON  PLU=ON  RESTENOSIS/OBI OR CORONARY RESTENOSIS/OBI

L15        68114 SEA ABB=ON  PLU=ON  L11 OR L14
L16          197 SEA ABB=ON  PLU=ON  L6 AND L15
L17      1429462 SEA ABB=ON  PLU=ON  1/SX,SC
L18          162 SEA ABB=ON  PLU=ON  L16 AND L17
L19           19 SEA ABB=ON  PLU=ON  PDE4D5/OBI OR PDE4/OBI(W)D5/OBI OR
                PDE4D7/OBI OR PDE4/OBI(W)D7/OBI
L20            1 SEA ABB=ON  PLU=ON  L18 AND L19
                D TI
L21            1 SEA ABB=ON  PLU=ON  L18 AND L1
L22        35469 SEA ABB=ON  PLU=ON  DRUG SCREENING/CT
L23        38363 SEA ABB=ON  PLU=ON  DRUG/OBI (2A) SCREEN?/OBI
L24        38363 SEA ABB=ON  PLU=ON  L22 OR L23
L25           13 SEA ABB=ON  PLU=ON  L18 AND L24
L26          104 SEA ABB=ON  PLU=ON  PERIPHERAL ARTERIAL OCCLUSIVE DISEASE/OBI
                OR PAOD/OBI
L27            0 SEA ABB=ON  PLU=ON  L18 AND L26

     FILE 'STNGUIDE' ENTERED AT 09:01:24 ON 06 JUN 2007

     FILE 'HCAPLUS' ENTERED AT 09:04:04 ON 06 JUN 2007
L28            QUE ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004 OR MY<2004
                OR REVIEW/DT
L29          120 SEA ABB=ON  PLU=ON  L18 AND L28
L30            1 SEA ABB=ON  PLU=ON  L29 AND L4
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L31           1 SEA ABB=ON  PLU=ON  L29 AND L19
L32         113 SEA ABB=ON  PLU=ON  L29 (L) (PAC OR PKT OR DMA OR BAC OR
                THU)/RL
L33       22632 SEA ABB=ON  PLU=ON  (INHIBIT?/OBI OR PREVENT?/OBI OR TREAT?/OBI
                ) (5A) L15
L34         113 SEA ABB=ON  PLU=ON  L32 AND L33
L35           7 SEA ABB=ON  PLU=ON  (L24 OR L26) AND L34
L36          13 SEA ABB=ON  PLU=ON  L35 OR L25
L37           7 SEA ABB=ON  PLU=ON  L36 AND L28
                D L37 TI 1-7

     FILE 'STNGUIDE' ENTERED AT 09:12:43 ON 06 JUN 2007

     FILE 'HCAPLUS' ENTERED AT 09:16:49 ON 06 JUN 2007
L38         113 SEA ABB=ON  PLU=ON  L32 AND L28
L39       47885 SEA ABB=ON  PLU=ON  RESTENOSIS/OBI OR ATHEROSCLEROSIS/OBI
L40          63 SEA ABB=ON  PLU=ON  L38 AND L39

     FILE 'STNGUIDE' ENTERED AT 09:18:09 ON 06 JUN 2007

     FILE 'HCAPLUS' ENTERED AT 09:21:58 ON 06 JUN 2007
L41        1066 SEA ABB=ON  PLU=ON  PHOSPHODIESTERASE#/OBI (2A) (TYPE 4/OBI OR
                4/OBI OR D/OBI OR D5/OBI OR D7/OBI)
L42          14 SEA ABB=ON  PLU=ON  L40 AND L41
L43          26 SEA ABB=ON  PLU=ON  L36 OR L37 OR L42
                SAVE L43 GIT181HCAP/A
                E FINGERLE J/AU
L44          29 SEA ABB=ON  PLU=ON  ("FINGERLE J"/AU OR "FINGERLE JUERGEN"/AU
                OR "FINGERLE JURGEN"/AU)
                E GULCHER J/AU
L45          99 SEA ABB=ON  PLU=ON  ("GULCHER J"/AU OR  "GULCHER JEFFREY"/AU
                OR "GULCHER JEFFREY R"/AU)
                E HIMBER J/AU
L46          29 SEA ABB=ON  PLU=ON  "HIMBER JACQUES"/AU
                E GRETARSDOTTIR S/AU
L47          23 SEA ABB=ON  PLU=ON  ("GRETARSDOTTIR S"/AU OR "GRETARSDOTTIR
                SOLVEIG"/AU OR "GRETARSODTTIR S"/AU)
L48         235 SEA ABB=ON  PLU=ON  L1 OR (L44 OR L45 OR L46 OR L47)
                E HOFFMAN (2A) ROCHE/PA,CS,CO
L49           0 SEA ABB=ON  PLU=ON  HOFFMANN/OBI (2A) ROCHE/PA
L50       18255 SEA ABB=ON  PLU=ON  HOFFMAN?/PA,CO,CS
L51       78933 SEA ABB=ON  PLU=ON  ROCHE?/PA,CO,CS
L52       16937 SEA ABB=ON  PLU=ON  L50 (L) L51
L53          43 SEA ABB=ON  PLU=ON  L52 AND L48
L54          27 SEA ABB=ON  PLU=ON  L53 AND L28
L55          26 SEA ABB=ON  PLU=ON  L54 NOT L43
                D AU 1-5
L56           0 SEA ABB=ON  PLU=ON  L1 AND L44 AND L45 AND L46 AND L47
                SAVE L55 GIT181HCAIN/A

     FILE 'REGISTRY' ENTERED AT 09:38:29 ON 06 JUN 2007
L57           0 SEA ABB=ON  PLU=ON  L5 AND MEDLINE/LC
L58           1 SEA ABB=ON  PLU=ON  L5 AND BIOSIS/LC
L59           1 SEA ABB=ON  PLU=ON  L5 AND EMBASE/LC
L60           0 SEA ABB=ON  PLU=ON  L5 AND DRUGU/LC

     FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 09:39:41 ON 06 JUN 2007
L61        6519 SEA ABB=ON  PLU=ON  L6
L62          40 SEA ABB=ON  PLU=ON  L61 AND L15
L63          32 SEA ABB=ON  PLU=ON  L62 AND L28
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